Early ADT May Not Improve Overall Survival in Prostate Cancer with PSA Relapse

Early initiation of continuous androgen-deprivation therapy (ADT) for prostate cancer (PCa) patients who experience biochemical relapse (BCR) may not meaningfully improve overall survival (OS), according to new findings. A retrospective analysis with data from 2 institutions found that metastasis-free survival (MFS) and OS were quite long among those who delayed hormone therapy. Among men who experienced BCR and whose PSA doubling time (PSADT) was <6 months, median MFS was 144 months; for those whose PSADT was <10 months, median MFS was 192 months. Median OS was 168 months and 204 months, respectively.

“These results are in line with the estimated survival times of men treated in contemporary trials of anti-androgens for nmCRPC [nonmetastatic castration-resistant prostate cancer],” observe the authors, who were led by Catherine Handy Marshall, MD, MPH, of Johns Hopkins University School of Medicine, Baltimore, MD.

“Prospective randomized data would provide the best evidence, but without that we are left with retrospective data,” said Marshall. “But it should be a discussion between patients and providers about whether or not to start ADT, because not starting it right at the time of BCR is a reasonable choice too.”

The study was published in The Journal of Urology (Vol. 206, pp. 623-629, 2021).

BCR is defined as a rise in PSA to 0.2 ng/mL and a confirmatory

(Continued on page 4)
Stereotactic Body RT Proved Better Than External Beam RT for Alleviating Pain in Cancer Patients with Spinal Metastases

Stereotactic body radiotherapy (SBRT) was superior to external beam RT (EBRT) for alleviating pain in cancer patients with metastases, according to a study published in The Lancet Oncology (Vol. 22, pp. 1023–133, 2021).

In a phase 2/3, randomized trial (ClinicalTrials.gov Identifier: NCT02512965), researchers sought to determine whether SBRT could improve the complete response (CR) rate for pain at a specific site of spinal metastasis, compared with conventional EBRT.

The intention-to-treat analysis included 229 men with painful, MRI-confirmed spinal metastases. They had a range of primary malignancies, including breast, lung, genitourinary, gastrointestinal, renal cell, and head and neck cancers, as well as melanoma and other cancers.

Half of patients (n=114) were assigned to SBRT (24 Gy in 2 daily fractions), and the other half (n=115) were assigned to EBRT (20 Gy in 5 daily fractions). The median follow-up was 6.7 months. The primary endpoint was the proportion of patients with a CR for pain at 3 months after RT.

At 3 months, the CR rate was 35% in the SBRT arm and 14% in the EBRT arm (risk ratio, 1.33; 95% Confidence Interval [CI], 1.14–1.55; P=0.0002). This significance in CR was maintained in multivariable analyses (odds ratio, 3.47; 95% CI, 1.77–6.80; P=0.0003).

At 3 months, the RT site-specific, progression-free survival rate was 86% in the EBRT arm and 92% in the SBRT arm (P=0.18, difference is not statistically significant). The overall survival rate at 3 months was 89 and 93%, respectively (P=0.33).

The Prognostic Association of Prostate MRI PI-RADS v2 Assessment Category and Risk of Biochemical Recurrence After Definitive Local Therapy for Prostate Cancer: A Systematic Review and Meta-Analysis

Rajwa P, Mori K, Huebner NA, et al.

Purpose: Although the Prostate Imaging—Reporting and Data System™ version 2 (PI-RADS™ v2) is a reliable diagnostic tool for significant prostate cancer (PCa), less is known about the prognostic significance of the structured reporting scheme for estimating oncologic outcomes after treatment. We aimed to synthesize the available evidence regarding the association of PI-RADS v2 score and risk of biochemical recurrence (BCR) among patients undergoing primary definitive treatment for PCa.

Materials and Methods: We systematically queried the PubMed® and Web of Science™ databases to identify studies addressing the association between the PI-RADS v2 and treatment outcomes. We included studies through November 2020 that assessed the independent prognostic significance of PI-RADS v2. After a risk assessment of bias and quality, we conducted a formal meta-analysis to estimate the pooled effects of prostate magnetic resonance imaging (MRI) classification on the risk of BCR.

Results: We identified 9 and 7 eligible studies including 2,274 and 1,215 men for the systematic review and meta-analysis, respectively. Eight were conducted in the context of radical prostatectomy (RP) and 1 post-radiation. Among patients treated with RP, higher PI-RADS v2 scores were significantly associated with risk of BCR (pooled Hazard Ratio [HR] 3.06, 95% Confidence Interval [CI] 2.16–4.33; p <0.01). There was no significant heterogeneity among studies. For all studies, PI-RADS v2 score remained significantly associated with BCR (pooled HR 3.19, 95% CI 2.28–4.45; p <0.01).

Conclusions: Prostate MRI findings assessed with the PI-RADS v2 classification were independently associated with risk of BCR after definitive local therapy, primarily based on data from RP. These findings support the prognostic significance of MRI, in addition to its role in PCa diagnosis.
You want beauty? Okay, how about going for a long run in the woods on a cool late summer morning with hints of fall colors begging for your attention? That is a thing of beauty, and it was the exercise I just finished before sitting down to write this column. Another thing of beauty was the recently published study in the highly reputable and competitive medical journal JAMA Oncology. The study was short (12 weeks) and small (52 participants), but it was AWESOME, and I mean really awesome (I like to repeat things twice when I want attention... attention). It exemplifies the beauty of exercise, or any heart healthy behavior when someone commits to it, and then sees it for the potential power it could have in your life and even for those around you.

The study was done at the University of Alberta, in Edmonton, Canada. It is a beautiful place, but I have also been there in the middle of winter, and it is kind of like getting free prostate cryotherapy every single time you step outside of your rent-a-car or hotel building, but I digress. Officially, the study was called “ERASE” (Exercise During Active Surveillance for Prostate Cancer) and the intervention group was assigned high-intensity interval training (HIIT) 3 times a week while the control group simply maintained their normal level of exercise. The goal was to FIRST increase cardiopulmonary fitness (CRF), and it impressively and significantly (p=0.01) accomplished this goal, and there were also significant decreases in PSA, PSA velocity, and other potential benefits.

Essentially, what made this exercise study so brilliant was not the type of exercise participants completed, but rather the primary goal of the lifestyle study was to first promote heart health and then everything else was “low-calorie gravy” so to speak. In the article, the authors mention that in some studies men on active surveillance (AS) have 3 times the risk of dying of cardiovascular disease (CVD) compared to prostate cancer (CaP) and, in fact, CVD is arguably the number 1 cause of death in CaP patients because it is still so darn common. Furthermore, one of the more common causes of morbidity and mortality in men with advanced CaP (apart from CaP itself) is CVD. It is common, and it is true that, ironically, many of the most amazing cancer drugs today also have the ability, in some cases, to raise CVD risk.

Thus, if you want to have men with CaP change their lives and reduce the side effects of the amazing treatments out there, then we need to encourage them to become heart healthier, not only through diet, but also through many other ways including exercise. When you perform heart healthy behaviors, you should always win on some level because you are improving the cornerstone or nucleus of your health (heart), which then has the capacity to potentially improve your body and mind from head-to-toe. I like occasional HIIT exercises so, for example, about once a week I like to sprint or run as fast as I can on a track or elliptical machine for 2 minutes with several minutes rest or cool down, and then I go all out again 3 to 5 times with intervals of rest again, but HIIT comes in all shapes and sizes and can be done in countless ways with any exercise (walking, swimming, kayaking, etc.). The most important thing you can do before starting any HIIT program is to absolutely check with your doctor to make sure you are fit enough to try it, because it is a good deal of initial stress on the heart and body.

Still, what happens when you break a sweat via any exercise is an endorphin release (“runners high” without the THC or CBD or XYZ) and I have personally enjoyed this experience several times a week since I was a kid. There is nothing, and I mean nothing, like it (except of course ice cream). Seriously, exercise promotes calmness, serenity, peace, love, and elevates your mood. It is the reason people like to say they “never regret a workout” after the workout is completed. It is the reason I would tell our kids when they were young or even my colleagues when they were or are cranky, that they are only one workout away from being nicer to me and others around them. In fact, I do not think we should have any more Zoom meetings unless all the participants exercise right before getting on the computer. World leaders should never get together or negotiate anything unless they were first forced to exercise right before their encounters.

I often wonder where my incredible marriage would be today if not for the fact that I, and my better 51%, love to work out... sometimes together and sometimes alone. No one should ever be allowed to argue unless they first had a workout. If I ever run for Congress or President (which will happen when the hottest sauna freezes over... if you get my drift) then I would reinstate the importance of fitness in the schools, at the workplace, before getting on an airplane... because it would make us all better, nicer, and more compassionate people. I can see it now... my first trademarked bumper sticker: “Health Care for All — Including Exercise — Vote Moyad.” Oh yeah baby! Speaking of babies... exercise would also be free for all babies too, especially right before I hold them on the campaign trail.

Reference:

PROSTATE CANCER HELPLINE: 1-800-808-7866 WWW.US TOO.ORG
value of ≥0.2 ng/mL following radical prostatectomy (RP), or a rise of ≥2 ng/mL above the nadir (lowest) PSA after radiotherapy (RT). “Not all men whose PSA level rises will develop metastases, and there is a lack of high-level evidence supporting the use of continuous ADT alone in the setting of PSA relapse,” the authors note.

The team further described the men that they studied: “We sought to examine what the life expectancy is in a cohort of patients who developed BCR but were not immediately treated with ADT... and therefore could not develop nmCRPC.” Notably, patients in the study were considered to be at high risk because of the time frame of their relapse (≤10 months).

Early initiation of continuous ADT in men with PCa who experience BCR has led to a new paradigm, nmCRPC, the authors point out. The practice of initiating early ADT remains unsubstantiated by level I evidence. Reports on the natural history of men with BCR indicate that these patients are heterogeneous in terms of natural progression of metastasis and survival.

Importantly, because these patients typically survive for many years and have virtually no symptoms until metastasis, factors regarding quality of life are crucial, inasmuch as ADT is associated with significant side effects and major costs.

In this study, Marshall and colleagues examined the outcomes for men with biochemically recurrent PCa for whom ADT was delayed until time of metastasis. The cohort included 806 men from two medical centers who underwent RP for clinically localized PCa and whose PSA doubling time was ≤10 months. The primary endpoints were MFS and OS from time of local treatment among men for whom ADT was delayed until time of metastasis.

The median age of the cohort was 61 years, most men were Caucasian (79%), and 38% had positive surgical margins; 17% had a Gleason score of ≤6, 54% had a Gleason score of 7, and 29% had a Gleason score of 8-10. Median PSA doubling time was 5.6 months, and the median follow-up was 9 years.

In multivariable analysis, Black race was associated with a lower risk for metastasis compared to White race (hazard ratio [HR], 0.5). Time from RP to BCR correlated with the risk of developing metastatic disease (HR, 0.8). A PSADT of <6 months was associated with a higher risk of developing metastatic disease vs. a PSADT of 6-10 months (HR, 3.2). Older age, higher pathologic T stage, higher Gleason sum, and faster PSADT were all associated with higher likelihood of death.

In an accompanying editorial, David VanderWeele, MD, and Maha Hussain, MD, both from the Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Chicago, Illinois, note that the question of how best to manage BCR remains controversial.

The current study adds to this debate, and “these data provide context for men with BCR and providers on whether to undergo ADT for years despite unproven benefit and quality of life impact,” they write. “New imaging may help or further add to the controversy, since biochemical response patients may have metastases on newer imaging.”

Until definitive data are available, they advise that these patients “be counselled regarding the lack of data to support ADT benefit in non-metastatic BCR.”

Association Between Lesion Location and Oncologic Outcomes After Focal Therapy for Localized Prostate Cancer Using Either High Intensity Focused Ultrasound or Cryotherapy


J Urol 206: 638-645, 2021

Purpose: We assessed whether prostate cancer (PCa) location might affect oncologic outcomes after focal therapy (FT) for PCa.

Materials and Methods: We identified 274 men receiving FT for PCa using either high intensity focused ultrasound (HIFU) or cryotherapy at a high volume center between 2009 and 2018. Survival analyses using the Kaplan-Meier method were used to assess any additional treatment and radical treatment rates according to PCa location. Propensity-score match analysis was used to compare oncologic outcomes of HIFU vs. cryotherapy according to PCa location. Covariates were PSA, clinical stage, prostate volume, Gleason score, maximum cancer core length, percentage of positive cores and treatment modality.

Results: A total of 166 and 108 men received FT with HIFU and cryotherapy, respectively. Overall, 39% (106) and 31% (85) received at least an additional treatment or a radical treatment after FT, respectively, with a median follow-up of 51 months. At 36 months’ follow-up, the rates of any additional treatment-free survival were 71%, 75%, and 69% for men with basal, mid-prostate and apical disease, respectively (p=0.7). At multivariable logistic regression analysis, PCa location was not significantly associated with higher risk of either any additional treatment or radical treatment (all p >0.4). After matching, there was no difference between HIFU vs. cryotherapy in terms of any additional treatment rates according to PCa location.

Conclusions: The PCa location does not significantly affect the rate of failure after FT. The presence of an apical lesion should not be considered an exclusion criteria for FT. Both HIFU and cryotherapy likely achieve similar medium-term oncologic results regardless of PCa location.
The PTEN-PI3K-AKT pathway is among the most frequently dysregulated oncogenic pathways in metastatic castration-resistant prostate cancer (mCRPC). Multiple inhibitors of this pathway are in late-phase development. However, patient response to this therapy is highly variable.

Identifying the best candidates for this treatment is important, researchers recently noted in a study in JCO Precision Oncology.

Arun Azad, PhD, of the Peter MacCallum Cancer Centre in Parkville, Australia, and colleagues used a novel circulating tumor DNA assay to identify such patients. In two independent prospective clinical cohorts totaling 231 men with mCRPC, the investigators found PTEN loss in 37% of patients, similar to the prevalence observed in tumor tissue. The team also observed poorer outcomes in men with PTEN-PI3K-AKT pathway aberrations, including those with dual PTEN loss and PIK3CA gain.

In addition, the researchers found that approximately one fifth of PTEN-neutral patients had other activating aberrations in the PTEN-PI3K-AKT pathway. “Plasma cfDNA profiling may facilitate and optimize patient selection for targeted treatment with AKT inhibitors in mCRPC,” the authors wrote.

In the following interview, Azad, associate professor of urological and prostate cancers, discussed the details and implications of the study, as well as future directions for research.

ASCO: Are liquid biopsies preferable to archival tumor samples for PTEN detection in patients with advanced prostate cancer (PCa)?

Azad: I would not go so far as to say liquid biopsies are preferable to archival tumor samples. Both have their place. PTEN loss is an early event in PCa evolution and therefore is typically seen in localized/early stage disease (when archival tumor samples are typically obtained). However, sometimes archival tumor tissue is not available, or is difficult to locate or retrieve, or insufficient material is available after diagnostic reporting has been undertaken.

In these cases, cfDNA is a pragmatic alternative to archival tumor tissue. An additional advantage for cfDNA over archival tumor samples is that other genomic alterations that activate the PI3K pathway are “later” events in PCa evolution (e.g., PIK3CA alterations) and these are more likely detected in a contemporaneous cfDNA sample than archival tumor tissue.

ASCO: Can you tell us about the targeted, high-sensitivity, next-generation sequencing cfDNA assay you used in your study? How does it differ from other cfDNA assays? – Feel free to get technical!

Azad: A key strength of this cfDNA assay is the capacity to detect copy number variations [CNVs] (gains, amplification, and losses). This really sets it apart from most other cfDNA assays, especially commercially available assays. Optimal detection of CNVs results from proprietary operation chemistry and analyses algorithms as well as the use of probes targeting single nucleotide polymorphisms in introns upstream and downstream of specific genes to capture additional copy number information.

This is crucial in prostate cancer, which is a disease characterized by relatively low mutational burden but a far higher proportion of CNVs. Most other available cfDNA assays significantly under-report CNVs, including in PTEN.

ASCO: Your study found that approximately one-fifth of PTEN-neutral patients had other activating aberrations in the PTEN-PI3K-AKT pathway. Can you tell us more about this finding and its implications?

Azad: In the IPATential study (abiraterone vs. abiraterone+ ipatasertib, an AKT inhibitor), an improvement in radiographic progression-free survival (rpFS) was seen with the addition of ipatasertib in PTEN-null mCRPC. The benefit was statistically significant, but relatively modest in absolute terms – median improvement of approximately 2 months. Nevertheless, this study shows the potential value in targeting AKT in mCRPC with activation of the PI3K pathway.

At the same time, while PTEN alterations are the most common mechanism underlying PI3K pathway activation, there are multiple other factors that regulate PI3K signaling. In this study, we found that in cfDNA from PTEN-neutral mCRPC patients, 21% had another genomic alteration that results in PI3K pathway activation. The most frequent of these other activating aberrations were PIK3CA mutation/gain and PTEN mutations.

This is a key finding, as it raises the possibility that ipatasertib and other AKT inhibitors may have a broader role in mCRPC patients beyond just those with PTEN copy number loss. This requires further evaluation but could play a key role in optimizing the use of AKT inhibitors in the future.

ASCO: Is there anything else you want to make sure oncologists understand about your study?

Azad: I hope they will see the value of using cfDNA for molecular profiling in mCRPC, and that it may ultimately become a substitute for using archival tumor tissue or obtaining fresh metastatic tissue, which is difficult, invasive, and painful. cfDNA is easy to obtain, and technology has rapidly moved forward so that even CNVs in key genes like PTEN can be readily detected.

ASCO: Do you plan any additional research in this area?

Azad: We certainly do. I have been involved in cfDNA/liquid biopsy research for nearly 8 years and we have shown a clear link between genomic alterations in cfDNA and outcomes with various systemic therapies used in advanced PCa including androgen receptor pathway inhibitors (like abiraterone and enzalutamide), taxane chemotherapy (docetaxel and cabazitaxel), and also molecularly targeted therapies.

With the addition of new drugs to the therapeutic armamentarium like olaparib and Lu 177 PSMA, there will be an ongoing need to identify biomarkers linked to clinical outcomes in mCRPC. A particular challenge will be identifying not just prognostic biomarkers, but also predictive biomarkers directly linked to outcomes with specific agents.

Reference
Kwan EM, et al. JCO Precis Oncol 5: 622-637, 2021

MedPage Today
04 August 2021
Routine Use of Focal Therapy for PCa in Next 5 Years (Continued from page 1)

ultrasound (HIFU): this approach now has a Current Procedural Terminology (CPT) code from the US Centers for Medicare & Medicaid Services

Medscape Medical News reached out to Matthew Cooperberg, MD, MPH, a urologist at the University of California San Francisco (UCSF), for comments about the essay’s optimism; he has questioned focal therapy in the past because of a lack of strong supporting evidence.

“While ‘routine’ is a bit of a vague term, now that HIFU has a CPT code, I do expect its use will, in fact, increase in the next 5 years,” Cooperberg wrote in an email. “The question is whether its use will increase appropriately.

“The challenge with focal therapy — regardless of energy modality — remains patient selection and accurate ablation zone definition,” he added.

Notably, UCSF has launched a new HIFU program — and Cooperberg has referred selected patients. “I’m both enthusiastic and cautious about the future, and we need to track our outcomes very closely across various practice settings,” he said.

“The goal of focal therapy is to treat only the area with the most aggressive tumor, known as the index tumor, while leaving the remaining gland and its surrounding structures alone,” according to Derek Lomas, MD, PharmD, a urologist at the Mayo Clinic in Rochester, Minnesota, in an explanatory article. “This approach is widely accepted in other types of cancer. For example, we commonly treat kidney cancers by removing or ablating only the tumor while leaving the rest of the kidney intact.”

However, some focal therapies also include approaches known as hemiablations, in which a full half of the prostate is destroyed, and approaches that leave very little of the gland behind.

Each of the modalities used for focal therapy has “unique indications, risks, and benefits and uses a different energy source for ablation,” Lebastchi and colleagues write in their essay.

They assert that focal therapy can provide oncological efficacy similar to radical prostatectomy or radiotherapy “while considerably reducing or even eliminating functional morbidities, such as incontinence and erectile dysfunction.”

Overall, they say focal therapy offers an opportunity for improved care because there is “an increasing body of emerging evidence demonstrating a favorable adverse effect profile with oncological control similar to whole-gland treatment options.”

In the essay, Lebastchi and colleagues point to a number of single-arm studies with encouraging efficacy and safety results. They also highlight a phase 3, randomized trial that they were involved in: this compared focal therapy (partial gland ablation with vascular-targeted photodynamic therapy) with active surveillance in early-stage disease, and uniformly showed better posttreatment biopsy (disease/no disease) and conversion-to-prostatectomy results with the focal therapy out to 4 years (J Urol. 2018;200:786-793).

However, that study did not have an active treatment comparator. For that gold standard, there is now anticipation for results from the CHRONOS trial in the United Kingdom, especially part A of the trial, which compares radical therapy to focal therapy (HIFU or cryotherapy), with 5-year progression-free survival as the primary outcome. That trial is slated for completion in 2027.

Until then, the lack of prospective randomized clinical trials and long-term follow-up “hinder acceptance [of focal therapy] in the urology community,” the essay authors comment.

Meanwhile, careful patient selection is very important, they say. The latest relevant guidelines state that appropriate candidates are men with a solitary, well-defined index lesion; patients with bilateral multifocal lesions; or very advanced tumors that are not appropriate for the focal approach.

A multidisciplinary international expert panel recently convened to establish guidance for clinicians offering focal therapies and then published a consensus statement to advise practitioners and researchers.

UCSF’s Cooperberg sees plenty of room for improvement among focal therapy practitioners and investigators. “From an outcomes standpoint, follow-up protocols and definitions of success remain inconsistent. I believe we’re making progress in all these areas but we’re not there yet,” he says.

“To date, some patients have been managed poorly,” Cooperberg added. “We certainly see many patients who have been inadequately counseled as to HIFU’s advantages and disadvantages, with sometimes disastrous results.”

Some of those unfortunate results may have arisen from the US Food and Drug Administration’s initial approval of HIFU in 2015, which was for use in ablating prostate tissue in general and not cancer specifically. This approval generated confusion, one expert commented at the time: “The FDA doesn’t specify whether it’s for benign or malignant disease; it’s a bit vague, like saying you can drive this car but we’re not going to tell you how to drive it,” said Manoj Monga, MD, from the Cleveland Clinic.

Medscape Medical News
06 August 2021

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Androgen Receptor Inhibitors Likely Boost Survival in Older Men With Nonmetastatic Castration-Resistant Prostate Cancer

Androgen receptor inhibitors (ARIs) improved survival in men ages 80 and older with non-metastatic, castration-resistant prostate cancer (nmCRPC) in a pooled analysis reported by the US Food and Drug Administration in *The Lancet Oncology*.

“Older adults remain disproportionately underrepresented in most cancer clinical trials, due to a variety of factors, including restrictive eligibility criteria,” Dr. Jaleh Fallah of the FDA’s Center for Drug Evaluation and Research told *Reuters Health*. “There is biologic rationale to include older adults in all stages of cancer drug development, given the physiologic changes that naturally occur with aging. “Treatment decisions should be based on the patient’s overall clinical condition and not merely on the patient’s age,” she said. “The use of geriatric assessment tools can be helpful in assessing the potential risk of treatment-related adverse events and to implement appropriate risk-mitigation strategies to prevent such events as possible.”

As reported online in *The Lancet Oncology*, https://www.thelan cet.com/journals/anonc/article/PIIS1470-2245(21)00334-X/fulltext, Dr. Fallah and colleagues searched the literature through August 2020 and identified 3 randomized controlled trials that met the selection criteria. All men had an Eastern Cooperative Oncology Group performance status of 0-1, CRPC, PSA ≥ 2.0 ng/mL, PSA doubling time of 10 months or less, and no evidence of distant metastatic disease.

Younger men in the intervention and placebo groups had a median age of 71 and 74% were white; older men had a median age of 83 and 69% were white. Age effects on metastasis-free survival (MFS) and overall survival (OS) were assessed in the intent-to-treat population. Safety analyses were done in men who received at least one dose of study treatment. Between 2013 and 2018, across the 3 trials, 2,694 men were assigned to an ARI (apalutamide, enzalutamide, or darolutamide) and 1,423 were assigned to placebo. In older men, the estimated median MFS was 40 months in the ARI groups and 22 months in the placebo groups (adjusted hazard ratio [HR], 0.37); median OS was 54 vs. 49 months, respectively (adjusted HR, 0.79).

In younger men, the estimated median MFS was 41 and 16 months in the ARI and placebo groups, respectively (adjusted HR, 0.31); median OS was 74 vs. 61 months (adjusted HR, 0.69).

Grade 3 or worse adverse events were reported in 55% of older men in the intervention group and 41% of those on placebo. In younger men, 44% in the ARI groups and 30% of those on placebo experienced grade 3 or worse adverse events.

The most common grade 3-4 adverse events were hypertension, (8% of both older and younger men on ARIs vs. 6% of older placebo patients and 5% of younger); and fracture (5% of older patients on ARIs vs. 3% on placebo, and 3% vs. 1%, respectively, of those on placebo).

Dr. Ali Zhumkhawala, a urologic oncology surgeon at City of Hope in Duarte, CA, called the findings “clinically helpful,” noting, “the caveat is that patients who received the second-generation ARIs did show higher rates of severe adverse events. While the quality-of-life questionnaire did not show a downside to treatment with these medications, the higher risk of side effects needs to be taken into account and treatment should be personalized per patient.

“I would like to see this study, or a similar study, stratify these outcomes based on the specific medication used,” he said. “There are concerns about the use of enzalutamide in the elderly. I would like to see the adverse events, survival and questionnaire data broken down by which medication the patient received so that we can further assess which specific medicine works best in which age group.”

Cancer-Related Cognitive Impairment in Men with Prostate Cancer

According to an article published online in *BMJ Supportive & Palliative Care* (https://doi.org/10.1136/bmjpcare-2021-003098), subjective concerns of cancer-related cognitive impairment (CRCI) have a greater impact on patient experience than objective measurements in men with prostate cancer (PCa).

The prospective analysis included 24 new men with PCa receiving androgen deprivation therapy (ADT) and radiation therapy (RT) during the first 12 months of treatment. The participants completed subjective and objective assessments of cognition, sleep continuity, and measures of insomnia, fatigue, depression, and anxiety.

The results showed that 29% of men demonstrated impaired objective cognition, while a separate 29% experienced significant declines in subjective cognition during the first year of treatment. However, presence of objective measures of CRCI was unrelated to perceived CRCI. Having a perception of poor sleep, such as suffering from insomnia, low total sleep time, or sleep efficiency, was particularly noticeable for those men experiencing cognitive impairments during ADT and RT. The authors say that improving sleep, particularly with cognitive behavioral therapy for insomnia, may be a valuable target to improve CRCI in men with PCa.

These findings suggest that clinicians should be vigilant regarding patients’ subjective concerns since these appear critical to patient outcomes.

*Medscape Pharmacists*
10 August 2021
A PSA level above 10 ng/mL and possibly age greater than 70 years are significantly associated with an increased risk for prostate cancer-specific mortality (PCSM) among men treated with brachytherapy (BT) for intermediate-risk prostate cancer (PCa), regardless of whether they also receive androgen deprivation therapy (ADT), according to a study published online July 24 in *Urologic Oncology*.

David D. Yang, MD, of Dana-Farber Cancer Institute in Boston, MA and colleagues conducted a prospective cohort study of 1,920 men with biopsy Gleason 3+4 PCa who received BT. Of these, 1,420 received BT alone and 500 received BT plus ADT for a median of 4 months. Over a median follow-up period of 7.8 years, 284 men (14.8%) died. Of the 31 (10.9%) who died from PCa, 18 (58%) were in the BT-only group and 13 (42%) were in the BT-ADT group.

In the BT-only group, each 1% increase in positive biopsies (PPB) was significantly associated with a 1.5% increased risk for PCSM after adjusting for multiple variables, Dr. Yang’s team reported. A PSA level of 10.1-20.0 ng/mL was significantly associated with a 5.6-fold increased risk for PCSM vs. a PSA of 4.0-10.0 ng/mL. Age older than 70 years was significantly associated with a 3.7-fold increased risk for PCSM vs. age 70 years or younger.

In the BT plus ADT group, increasing PPB and older age were not significantly associated with increased PCSM risk. A PSA level of 10.1-20.0 ng/mL was significantly associated with a 4.2-fold increased risk for PCSM compared with a level of 4.0-10.0 ng/mL.

Noting that PPB was no longer associated with a significant increase in PCSM when a median of 4 months of ADT was added to BT, the investigators stated: “It may be that as the volume of disease as assessed on biopsy increases, the cytoreductive effects of ADT allow for more effective delivery of BT. “Should these findings be validated in future studies, then advanced imaging and targeted biopsy of suspicious areas should be investigated in an effort to personalize treatment and minimize the risk of PCSM in these men,” the authors concluded. *Renal & Urology News* 02 August 2021

### Death from Other Causes (Continued from page 1)

Men younger than 50 years without mPCa,“ Dr. Alhalabi’s team reported. Men with mPCa had a significant 34%, 31%, and 19% higher mortality rate from cardiovascular disease, cerebrovascular disease, and COPD, respectively, compared with the age-matched US male population in adjusted analyses, according to the investigators.

White patients and Asian and Pacific Islander patients had a significantly increased risk for death by suicide, whereas Black patients and American Indian and Alaska Native patients did not.

In an accompanying editorial, Samuel W.D. Merriel, MSc, of the University of Exeter Medical School in Exeter, UK, and coauthors commented, “Their finding of increased suicide rates among Asian or Pacific Island patients and White patients with mPCa is a surprise and should be investigated further, considering that such deaths are potentially preventable.” *Renal & Urology News* 13 August 2021

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It seems like I start out with a good erection and then I lose it during sex, and now I worry about losing my erection during sex. What can I do?

RESPONSE FROM DR. JEFFREY ALBAUGH:
Thank you for your question. Many things can affect your erections when you are trying to have sex with your partner, including anxiety or lack of focus during sex. When you get anxious, it causes a physical response from your body with increased adrenaline (which is a part of your body’s fight or flight response) and this may lead to losing your erection. When you are having sex, try to stay focused and mindful on sex and not worry. You want to stay focused on sex so you feel connected to your partner and you can enjoy yourselves. If other thoughts are trying to come into your mind, or you are getting anxious, breathe deeply and redirect your mind back towards sex and sexual thoughts only. Neither your partner or you need a hard penis to reach orgasm as men and women both can orgasm/climax without intercourse through oral stimulation, manual stimulation (rubbing genitals) and/or vibration on the genitals. It can be very helpful to talk with your partner about your fears and concerns about sex. Work together with your partner to have fun and please each other.

If you feel like you need more help with anxiety or other feelings about sex, it may help to meet with a sex therapist. You can find a therapist through the American Association of Sex Educators, Counselors and Therapists at www.aasect.org.


Watch Dr. Albaugh’s presentation on sexual health and intimacy from the Prostate Cancer Pathways for Patients and Caregivers event recorded at NorthShore University HealthSystem in Skokie, IL on November 3, 2018 at https://www.youtube.com/watch?v=Hiq0dDEb1l0&t=4483s.

Read previous issues of Between the Sheets at www.ustoo.org/BTS.

Do you have a question about sexual health or intimacy? If so, we invite you to send it to Us TOO. We’ll select questions to feature in future Between the Sheets columns.

Please email your question to: us too@ustoo.org

Or mail your letter to:
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An Update on Prostate MRI
By Janet Farrar Worthington

Dr. Peter Choyke of the National Cancer Institute offers perspective on the use of MRI in prostate cancer.

Can MRI really make a difference in diagnosing prostate cancer? One man experienced five inconclusive “TRUS” (transrectal ultrasound) biopsies before an MRI-guided fusion biopsy revealed Gleason 3 + 4 cancer. Today he is cancer-free.

“With TRUS, unfortunately, this story is all too common,” says radiologist Peter Choyke, M.D., Senior Investigator and Director of the National Cancer Institute’s Molecular Imaging Branch, and a pioneer in the rapidly evolving use of MRI to evaluate prostate cancer.

“To understand why,” he adds, “let’s look at what, until very recently, was state of the art: 12 biopsies performed by the urologist under TRUS, six on one side and six on the other. It really wasn’t targeted to anything in particular.” The basic biopsy sampled the upper, mid and lower part of each side of the prostate (this, by the way, was an improvement over the old biopsies of 20 years ago, which took only six samples!). Even with 12 samples, “there are a lot of opportunities to miss lesions. And, because urologists don’t want to injure the urethra, which is in the center of the prostate, they tend to put the needles more towards the back of the gland, so the front part of the gland was relatively unsampled in a traditional TRUS biopsy.”

In other words, the traditional biopsy is largely hit or miss. “Once we started doing MRIs,” says Choyke, “we realized that a lot of tumors are above where the needles usually went in; in fact, those lesions are more amenable to transperineal biopsy. That was important in helping us detect the cancers in men who had multiple negative TRUS-guided biopsies.”

A targeted biopsy – done with TRUS, but using the MRI as a roadmap – can direct the needle to specific areas that look suspicious. “Also, once you have the MRI, you realize how big the lesion is. With TRUS, you just had a specimen that was positive. You didn’t know if it came from a 3mm- or a 5 cm-sized lesion! It was just ‘positive.’ Now with MRI, we have a much better feel: is this a big lesion, has it been there a long time, has it grown outside the prostate, possibly to the lymph nodes? Are the seminal vesicles involved, is the bladder involved? There’s a lot of anatomy that you can get from the MRI that you just don’t get from the biopsy information. Was the needle in the center of the lesion, or the periphery – or did it biopsy something completely different than the main lesion? Is this cancer caught very early, so it’s hard to see, or is it large and obvious? That influences the discussion of treatment options, and allows the patient to make a much more informed decision. With MRI, you’re way far ahead of the game.”

And this is why Choyke believes that “in the best of all possible worlds, every man with suspected prostate cancer would get an MRI. MRI is of even more benefit,” he adds, “as a man’s PSA rises. We did a study where we compared men with a PSA less than 5 with men with a PSA greater than 5. For men with a lower PSA, the advantage of MRI was much smaller compared to a traditional TRUS biopsy. But for those with PSA greater than 5, it was clearly superior to have an MRI.”

That said, there are some qualifiers: Not every insurance policy pays for MRI, for instance, and good-quality MRI is not universally available. The power of the MRI machine itself used to matter more, with 3 Tesla strength preferred. But today, the major determinants are, “how old is the MRI unit, and is there a radiologist who is focused on prostate MRI, who has been to courses learning how to interpret it properly? Or, is the radiologist a generalist without specific expertise?” If you’re paying for part or all of the cost out-of-pocket, Choyke notes, “these scans are very expensive. I don’t think it’s unreasonable to ask good questions.”
The SEA Blue 2021 Prostate Cancer Walk and Run

SEA Blue is a celebration of life, of those who have risen to the challenge to fight prostate cancer, of the lives that have been lost to the disease, and of the people we will help to combat it in the future through Support, Education, Advocacy and Awareness (the SEA in SEA Blue).

Please Join Us For:

- Celebration Walk and 5K Run
- Prostate Cancer Education
- Entertainment
- Lunch and Refreshments
- Fundraising
- Emcee Steve Sanders, Former WGN News Anchor
- Prostate Cancer Survivor/Warrior Recognition
- Virtual Fundraising and Participation

Please help us raise money to help those affected by prostate cancer with Support, Education, Advocacy and Awareness at no charge.

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