Markers That Cause Toxic Radiotherapy Side Effects in Prostate Cancer Identified

A new study published online in the journal eBioMedicine by researchers from The University of Manchester looked at the genetic information of more than 1,500 prostate cancer patients and identified two variants linked to increased risk of radiotherapy (RT) side effects.

Nearly 50% of the 1.1 million men a year worldwide diagnosed with prostate cancer undergo RT. It is an effective treatment, but 10-50% of men suffer from RT side effects which can cause long-term problems with urination or rectal bleeding. It is not known why some men are more susceptible to side effects and, as a result, doses are kept low to minimize the risk in all patients – reducing the effectiveness of treatment. The new Radiogenomics Consortium study coordinated from Manchester, UK, aimed to identify if there were any genetic markers which could explain this.

Genetic profiling was carried out on 1,564 men from four centers based in Europe and North America. It examined genetic variants described as single nucleotide polymorphisms (SNPs), which form part of the subunits of DNA. Two years after the RT, 17.8% of the men suffered from rectal bleeding, 15% increased urinary frequency and 8.1% had a decrease in urine stream. Professor of Radiation Biology, Catharine West from The University of Manchester’s Institute of Cancer Sciences led the research. She said, “The first studies into SNPs were smaller. We wanted to determine if observational management like AS is underused in minority populations, particularly within the framework of an equal access health-care system,” she continued. “This is one of the few groups studied with sufficient sample sizes to examine whether the associations of clinical triggers for beginning active treatment varied by sociodemographic factors.”

The study included men who underwent radical prostatectomy (RP) or radiation therapy (RT). A new study published online in the journal eBioMedicine by researchers reported online in the Journal of Clinical Oncology on 1 August 2016.

“Although many previously published studies have demonstrated that administering SRT to prostate fossa at lower PSA values improved biochemical (PSA) control, the lack of data showing similar improvements in the incidence of metastases and or survival outcomes has tempered the enthusiasm of some clinicians to consider this treatment for men with detectable PSA following prostatectomy for prostate cancer,” said Dr. Bradley J. Stish from Mayo Clinic in Rochester, MN.

“We wanted to determine if observational management like AS is underused in minority populations, particularly within the framework of an equal access health-care system,” he continued. “This is one of the few groups studied with sufficient sample sizes to examine whether the associations of clinical triggers for beginning active treatment varied by sociodemographic factors.”

The study included men who (Continued on page 6)

Salvage Radiotherapy at Lower PSA Levels Tied to Better Prostate Cancer Outcomes

Salvage radiotherapy (SRT) beginning at lower PSA levels after radical prostatectomy (RP) is associated with improved outcomes in men with prostate cancer, researchers reported online in the Journal of Clinical Oncology on 1 August 2016.

“Although many previously published studies have demonstrated that administering SRT to prostate fossa at lower PSA values improved biochemical (PSA) control, the lack of data showing similar improvements in the incidence of metastases and or survival outcomes has tempered the enthusiasm of some clinicians to consider this treatment for men with detectable PSA following prostatectomy for prostate cancer,” said Dr. Bradley J. Stish from Mayo Clinic in Rochester, MN.

“Our study clearly demonstrates that even when controlling for well-validated prostate cancer risk factors, such as Gleason score and tumor stage, use of SRT when the PSA is lower is clearly associated with significant improvements in the clinically important patient outcomes of distant metastases, prostate cancer specific mortality (PCSM), and overall survival (OS),” he told Reuters Health by email.

Dr. Stish and colleagues investigated outcomes of SRT for 1,106 men with detectable PSA after RP for prostate cancer who were treated between 1987 and 2013. The median follow-up (Continued on page 2)
Robot-Assisted Laparoscopic Prostatectomy Versus Open Radical Retropubic Prostatectomy: Early Outcomes from a Randomised Controlled Phase 3 Study
Yaxley JW, Coughlin GD, Chambers SK, et al.

Background: The absence of trial data comparing robot-assisted laparoscopic prostatectomy (RALP) and open radical retropubic prostatectomy (RRP) is a crucial knowledge gap in uro-oncology. We aimed to compare these two approaches in terms of functional and oncological outcomes and report the early postoperative outcomes at 12 weeks.

Method: In this randomised controlled phase 3 study, men who had newly diagnosed clinically localised prostate cancer and who had chosen surgery as their treatment approach, were able to read and speak English, had no previous history of head injury, dementia, or psychiatric illness or no other concurrent cancer, had an estimated life expectancy of 10 years or more, and were aged between 35 years and 70 years or more, and were aged 25 years were eligible and recruited from the Royal Brisbane and Women's Hospital (Brisbane, QLD). Participants were randomly assigned (1:1) to receive either RALP or RRP. Randomisation was computer generated and occurred in blocks of ten. This was an open trial; however, study investigators involved in data analysis were masked to each patient's condition. Further, a masked central pathologist reviewed the biopsy and RP specimens. Primary outcomes were urinary function (urinary domain of EPIC) and sexual function (sexual domain of EPIC and IIEF) at six weeks, 12 weeks, and 24 months, and onctology outcomes such as biochemical progression and positive surgical margins at 10 years. The trial was powered to assess health-related and domain-specific quality of life outcomes over 24 months. We report here the early outcomes at six weeks and 12 weeks. The per-protocol populations were included in the primary and safety analyses. This trial was registered with the Australian New Zealand Clinical Trials Registry (ANZCTR), number ACTRN1261100061976.

Findings: Between Aug 23, 2010, and Nov 25, 2014, 326 men were enrolled, of whom 163 were randomly assigned to RRP and 163 to RALP. Eighteen withdrew (12 assigned to RRP and six assigned to RALP); thus, 151 in the RRP group proceeded to surgery and 157 in the RALP group. One-hundred twenty-one assigned to RRP completed the 12 week questionnaire vs. 131 assigned to RALP. Urinary function scores did not differ significantly between the RRP group and RALP group at six weeks post-surgery (74.5 vs. 71.1; p=0.09) or 12 weeks post-surgery (83.8 vs. 82.5; p=0.48). Sexual function scores did not differ significantly between the RRP and RALP groups at six weeks post-surgery (35.0 vs. 38.9; p=0.32; 37.2; p=0.45) or 12 weeks post-surgery (35.0 vs. 38.9; p=0.18). Equivalence testing on the difference between the proportion of positive surgical margins between the two groups (15 [10%] in the RRP group and 23 [15%] in the RALP group) showed that equality between the two techniques could not be established based on a 90% confidence interval (CI) with a difference of 10%. However, a superiority test showed that the two proportions were not significantly different (p=0.21). Fourteen patients (9%) in the RRP group vs. six (4%) in the RALP group had postoperative complications (p=0.052). Twelve (8%) men receiving RRP and three (2%) men receiving RALP experienced intraoperative adverse events.

Interpretation: These two techniques yielded similar functional outcomes at 12 weeks. Longer term follow-up is needed. In the interim, we encourage patients to choose an experienced surgeon they trust and with whom they have rapport, rather than a specific surgical approach.

Salvage RT Post-RP
(Continued from page 1)

was 8.9 years. The cumulative rate of biochemical recurrence (BCR) was 49.9% at five years and 64.3% at 10 years. For distant metastases, rates were 10.9% and 19.9%, respectively, and OS was 92.9% and 77.3%. PCSM was 3.0% at five years and 10.4% at 10 years, the team reported. In multivariable analyses, higher pre-SRT PSA levels (>0.5 ng/mL) were associated with significantly higher rates of BCR, distant metastases, and PCSM. Only OS did not appear to be different between pre-SRT PSA ≤0.5 ng/mL vs. >0.5 ng/mL. Higher SRT doses (≥68 Gy) and androgen deprivation therapy (ADT) were also identified as treatment factors that could reduce the risk of post-SRT BCR.

“These observations add to the growing body of literature reporting that benefits (Continued on page 8)
Doc Moyad’s What Works & What is Worthless Column, Also Known As “No Bogus Science” Column

“Step right up! Step right up! The Great Moyadini will guess the size of your prostate for less than 100 dollars?!!”

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.

Bottom Line:
It is interesting that from seed implants (SI), to external beam radiotherapy (RT), to active surveillance (AS), an accurate prostate size matters before you and your doctor can choose the best treatment for you. So, the next time you decide on treatment, you really need to ask your doctor for an accurate size of your prostate based on transrectal ultrasound (TRUS) and/or MRI, because the finger seems to work about as well as the person (aka “carny”) guessing your weight at the local carnival or amusement park!

Okay, why is diet, supplement and prevention dude (aka Mark Moyad) talking about prostate size? Has he lost his mind? Well, they say God plays a cruel joke on men as we age because just about everything gets smaller or recedes as men get older from head-to-toe except male breasts, bellies and prostates! Yikes! That is not funny!

So, why am I talking about prostate size? Well, it is because I am taking a stand and instead of shouting out of my window in protest, I have decided to protest with my column. It is still amazing to me how many men know all about their prostate cancer and all their numbers before picking a treatment, but do not know their prostate size. There are many places I could point my finger (no pun intended) as to why this is the case, but the point is that more and more research is showing the importance of getting an accurate prostate size before making a treatment decision.1

Today, it is more critical than ever to know, as precisely as possible, the size of your prostate. Think about it for a second. In order to qualify for active surveillance (AS), one of the key requirements is a PSA density ≤0.15. This can only be calculated with your PSA and a precise prostate size! In order to qualify for brachytherapy (and perhaps other treatments) you and your doctor need to know your prostate size!

Many primary care doctors guess the size with a finger which, from the latest studies, appears to be as good as a carnival person. So, you need the involvement of a urologist and/or oncologist. I decided to call my good friend, Dr. Mack Roach at the University of California at San Francisco (world famous radiation oncologist), and he reviewed with me the accuracy of MRI, and TRUS, both of which require no radiation, of course.

No dietary supplements can consistently shrink a large prostate if needed, but there are drugs that do it very well, from hormone therapy injections to finasteride (Proscar®) and dutasteride (Avodart®). Still, the bottom line is that so many men I meet know their PSA and pathology, get a second opinion on pathology, know their treatment options very well, but do not realize that knowing the ACCURATE size of their prostate is arguably as important as the decision to go on active surveillance (AS) or be treated because it is one of the key factors in AS!

Because September is prostate cancer awareness month, I thought it would be the best contribution I could provide to many men reading this column! So do YOU know the real size of your prostate? “Well, step right up and for only $99.99, the amazing Moyadini will guess it for you along with your weight, height and birthdate!” Send your money as a donation to Us TOO and, in no time, the great Moyadini will amaze you! We take all major credit cards or cash and even good cold beer for payment!

What are you waiting for?!!!

Reference:

Olanzapine (Zyprexa®) Prevents Chemotherapy-Induced Nausea (CIN)

The antipsychotic agent olanzapine (Zyprexa®) proved better for preventing nausea than placebo in a multicenter randomized, double-blind phase III trial appearing in the New England Journal of Medicine.

Patients undergoing highly emetic chemotherapy whose prophylactic drug combination included olanzapine were more likely than those who received a placebo-containing combination to have no nausea and vomiting in the early, later, and overall assessment periods or to experience no emesis at all, reported Rudolph M. Navari, MD, PhD, of Indiana University School of Medicine-South Bend, and colleagues.

The proportion of patients with no CIN was significantly greater with olanzapine than with standard prophylaxis plus placebo for the following three assessment periods: the first 24 hours after chemotherapy (74% vs. 45%), 25 to 120 hours after chemotherapy (42% vs. 25%), and the overall 120-hour period (37% vs. 22%).

Olanzapine works by blocking multiple neurotransmitters, including dopamine and serotonin, at various receptor sites, and blocking catecholamines, acetylcholine, and histamine.

The phase III trial randomized 380 cancer patients (mean age of 57, with 72.4% female and 90.3% of whom were white) enrolled during 2014-2015 at US academic and community treatment centers. The majority of the patients (63.7%) were being treated for breast cancer, followed by lung cancer (12.9%) and other malignancies (23.4%).

Patients had not previously received chemotherapy and were receiving cisplatin (270 mg/m² of body-surface area) or cyclophosphamide-doxorubicin. The study compared olanzapine with placebo in combination with dexamethasone, aprepitant or fosaprepitant, and a 5-hydroxytryptamine type 3 receptor antagonist.

The number of patients receiving drug combinations, given before and after chemotherapy, was similar in both arms: 192 for olanzapine and 188 for placebo. Both groups received either 10 mg of olanzapine orally or

(Continued on page 8)
Hydrogel Spacer Technology Reduces Rectal Radiation Side Effects Helping to Improve Quality of Life

By Eileen Gardner, RN — Augmenix, Inc.

Within the past several decades, the rate of survival among men with prostate cancer has improved significantly, thanks to a growing field of research and advanced treatments. Although many men diagnosed with prostate cancer will end up surviving the disease, the long-term side effects of the chosen treatment option often hinder quality of life (QoL). After initial diagnosis, the most pressing questions for these men then become, how will treatment impact my QoL? Does living longer mean living well?

A study published in the January 2013 issue of the New England Journal of Medicine found that there are, in fact, several long-lasting side effects following surgery and radiotherapy (RT). Findings confirmed that men having undergone RT or surgery were still experiencing urinary, bowel and sexual side effects lasting up to 15 years following treatment.

The Impact of Treatment on Quality of Life

Radical prostatectomy (RP) and prostate RT have been shown to be the two most successful treatments for low- and intermediate-grade prostate cancer. Historically, the most common complications following RP related to injury to the urinary system (incontinence, erectile dysfunction), while complications following prostate RT were often related to rectal radiation injury (bleeding, diarrhea). Now a new technology called the SpaceOAR System is available that reduces rectal injury during prostate RT, potentially simplifying the decision process for men when deciding which treatment to undergo.

Rectal injury can occur during prostate cancer radiation treatment because the rectum lies next to the prostate and can consequently receive high radiation doses. To reduce this injury, SpaceOAR hydrogel physically pushes the rectum away from the prostate during treatment, thereby reducing both the rectal radiation dose and side effects.

How does it work?

The hydrogel spacer is placed into position during a brief outpatient procedure under general, regional or local anesthesia prior to the start of RT. It is injected through a needle as a liquid where it creates approximately one-half inch of space between the prostate and rectum and then solidifies into a soft gel-like material. There is no serious discomfort other than a slight pinprick or pressure at the injection site. In a recent FDA study, no SpaceOAR hydrogel patients reported any long-lasting discomfort related to the implanted spacer. The hydrogel spacer stays in place for about three months before being naturally absorbed and cleared in the patient’s urine in approximately six months.

Because most cancers occur on the side of the prostate next to the rectum, delivering enough RT to kill the cancer while not injuring the rectum remains challenging. Several techniques have been developed to improve the RT process (e.g., gold markers to aid prostate visualization, patient positioning and a balloon inflated inside the rectum to reduce prostate motion).

Clinical Evidence and Safety

Clinical trials in the United States and Europe demonstrated that the hydrogel is safe, and that the space created significantly reduces the RT delivered to the rectum.

The randomized SpaceOAR System United States Clinical Trial found that men who received the hydrogel spacer reported significantly less rectal pain during RT and had significantly less severe long-term rectal complications. Only one in 49 patients experienced mild complications in the year following RT.

The control patients (who did not receive the hydrogel spacer) were 3.5 times more likely to develop long-term rectal complications than hydrogel spacer patients.

Similar to hydrogel products used on the brain, eyes and vascular system, SpaceOAR is composed of biocompatible material that can be used safely in the body.

A Little Space Makes a Big Difference™

In addition to reducing rectal complications following prostate RT, hydrogel spacers should allow physicians to give more radiation per day, resulting in the completion of treatment in fewer visits (hypofractionation). This can result in both improved convenience to the patient and healthcare savings. Additionally, with less fear of rectal injury, physicians may be able to deliver more RT to the prostate to potentially decrease rates of cancer recurrence. Finally, the ability to create space may allow physicians to give additional RT to men with recurrent prostate cancer, giving those patients another treatment option.

Since SpaceOAR received FDA clearance in April 2015, many centers across the United States are offering SpaceOAR with encouraging results. Going forward, it may become standard-of-care in prostate RT, potentially reducing rectal side effects and allowing for dose escalation, hypofractionation, and new treatment options for men with recurrent prostate cancer.

Editors’ note: Content of this article was reviewed and edited for inclusion in the Us TOO Hot SHEET, but please recognize that the information provided about the SpaceOAR device is written by Augmenix Inc.

Indication: SpaceOAR System is intended to temporarily position the anterior rectal wall away from the prostate during RT for prostate cancer and in creating this space it is the intent of SpaceOAR System to reduce the radiation dose delivered to the anterior rectum. The SpaceOAR System is composed of biodegradable material and maintains space for the entire course of prostate RT and is completely absorbed by the patient’s body over time.

Potential complications: While rare, the following events theoretically may occur with SpaceOAR System: pain associated with SpaceOAR hydrogel injection; pain or discomfort associated with SpaceOAR hydrogel; needle penetration of the bladder, prostate, rectal wall, rectum, or urethra; injection of SpaceOAR hydrogel into bladder, prostate, rectal wall, rectum, or urethra; local inflammatory reactions; infection; injection of air, fluid, or SpaceOAR hydrogel intravascularly; urinary retention; rectal mucosal damage, ulcers, necrosis; bleeding; constipation; and rectal urgency.

www.spaceoar.com
Brouhaha About Metastatic Prostate Cancer in the United States

Recently, major news outlets such as CBS, Newsweek, and Chicago Tribune reported what many US urologists have feared and anticipated: that a study showed metastatic prostate cancer (mPCa) was on the rise in the United States. Some of the media coverage also indicated that controversial recommendations, which have led to less prostate-specific antigen (PSA) testing, were to blame, at least in part.

The study did not prove either point, said critics, including, most prominently, Otis Brawley, MD, the chief medical officer of the American Cancer Society, who dissects both the study and the popular interpretation of its results.

Dr. Brawley, quoted in an article in the Philadelphia Inquirer, said “it is very possible” that less early detection will result in a higher rate of advanced disease. Nevertheless, “they simply did not prove it,” he also said about the new study.

The source of the controversy was an analysis published July 19th in Prostate Cancer and Prostatic Diseases.

In the study, researchers from Northwestern University and the University of Chicago, IL, identified all newly diagnosed cases of prostate cancer from 2004 to 2013 in the National Cancer Data Base (NCDB) at 1,089 different healthcare facilities in the United States.

They reported that the annual number of newly diagnosed cases of mPCa increased in the latter years of the study period, from 2007 to 2013 (with an annual percentage change of 7.1%, P <0.05). Also, they highlighted the fact that the annual number of newly diagnosed cases was 72% higher in 2013 (than in 2004 (2,890 vs. 1,685, respectively). A Northwestern University press release described this increase as a “skyrocket.”

Also, the investigators found that the median PSA of men who were diagnosed with metastatic prostate cancer increased from 25.5 ng/mL in 2004 to 49.7 ng/mL in 2013, which is an indicator of a greater extent of disease at diagnosis, according to the press statement.

In their study’s discussion section, the authors state that the “social and biologic factors underlying these PSA escapes and rising mPCa cases are unknown.”

But a rise in aggressive cancers has been predicted by many experts to be an eventual outcome of the United States Preventive Services Task Force (USPSTF) guidance from both 2008 that recommended against routine PSA screening in men older than 75 years and 2012 that recommended against routine PSA screening in all healthy men.

In a press statement, senior study author Edward Schaeffer, MD, chair of urology at Northwestern University Feinberg School of Medicine, said, “One hypothesis is the disease has become more aggressive, regardless of the change in screening. The other idea is since screening guidelines have become more lax, when men do get diagnosed, it’s at a more advanced stage of disease. Probably both are true. We don’t know for sure but this is the focus of our current work.”

In the study, the authors conclude: “It is likely that trends in the National Cancer Data Base reflect national patterns.” However, Dr. Brawley, writing a post on the ACS media blog, said that the study design does not allow one to conclude that the rate of mPCa is increasing in the US population.

“The way epidemiologists measure things like incidence and mortality is to study rates, the number of cases per a number of people (usually per 100,000) to look for trends. But this study, done by a group of urologists, didn’t do that. Rather than measure rates of mPCa, they looked at the number of cases. That is far from the same thing,” he wrote.

The researchers acknowledged this problem to some degree. “Limitations to the current study include the lack of national annual incidence rates in the NCDB,” they write. However, they do not explain the significance of that missing data or discuss the crucial difference between incidence (i.e., the number of cases) and incidence rates.

“The increased number of cases could have various explanations,” stated Dr. Brawley. “Epidemiologists learned long ago that you can’t simply look at raw numbers. A rising number of cases can be due simply to a growing and aging population, among other factors,” he said.

Another expert expressed similar doubts about the study in an article in the New York Times titled “Flawed Study of Advanced Prostate Cancer Spreads False Alarm.” Christopher Filson, MD, an assistant professor of urology at Emory University School of Medicine, Atlanta, GA, said, “I don’t want to claim their results are wrong. They may be true, but the way they looked at the question brings in too many possible alternative explanations.”

Medscape Medical News 29 July 2016

Cancer Survival Worse in RA Patients

Survival was more than two years shorter in breast and prostate cancers

Patients with rheumatoid arthritis (RA) had a 40% to 50% increased mortality risk if they developed breast or prostate cancer, a large, population-based study found.

Compared with individuals without RA, those previously diagnosed with RA had an adjusted hazard ratio (HR) for mortality of 1.41 (95% CI 1.21 to 1.65, P<0.0001) for breast cancer and 1.53 (95% CI 1.26 to 1.85, P<0.0001) for prostate cancer, according to Maria E. Suarez-Almazor, MD, PhD, of the MD Anderson Cancer Center in Houston, TX, and colleagues.

For colorectal cancer, a significantly decreased survival was seen after adjustment for demographics and tumor stage, but not after controlling for comorbidities other than RA (HR 1.15, 95% CI 0.99 to 1.34). And for lung cancer, there was no survival difference among those with or without RA (HR 1.01, 95% CI 0.92 to 1.12), the researchers reported online in Arthritis Care & Research.

“These findings suggest that the additional cancer mortality risk from having RA is more pronounced for those tumors with longer expected median survival,” they wrote.

Patients with RA reportedly have an increased risk for lung cancer and lymphoma, according to a meta-analysis, but appear to have a lower risk for breast cancer, possibly because of hormonal factors, and colorectal cancer, because of the protective effects of nonsteroidal anti-inflammatory drugs.

Most earlier studies evaluating the effects of comorbid-
Radiotherapy Side Effects
(Continued from page 1)

cinetic variants. Centers give RT in different ways and we needed to show this variability was not a problem.”
The two variants found were associated with an increased frequency of urinating and decreased urine flow. Causes for the associations are unclear, but the two SNPs identified are located in the gene regions that are expressed in tissues exposed to RT.

Results show RT cohorts can be combined and larger studies should identify enough variants to develop a test to predict a cancer patient’s risk of RT-induced side effects.

Professor West added, “There are currently more than 32 million people alive five years after having cancer, so the side effects of their treatment are an important issue for them. If we can develop a test that means people can reduce the risk of these problems that will be of huge benefit to this group.”

MedicalNewsToday.com
27 July 2016

Cancer Survival Worse in Rheumatoid Arthritis Patients
(Continued from page 5)

ities on cancer survival have considered overall comorbidities, rather than any individual coexisting condition, including RA. To examine the effects of previously diagnosed RA on survival in four common solid tumors, Suarez-Almazor and colleagues analyzed data from the Texas Cancer Registry and the Medicare claims database for patients diagnosed with one of these malignancies between 2001 and 2010.

The linked Medicare and Texas registry included 697,734 patients with cancer diagnosed during the study period, with 139,097 having one of the four specified malignancies. A total of 1.1% had two or more RA claims. Mean age at the time of cancer diagnosis was 76. Those with RA were more often women, had more comorbidities, resided in areas with lower income, and more often had their cancer diagnosed at regional or distant stages than those without RA (40% vs. 34%, P=0.0003).

A total of 3.3% of patients with breast cancer had one or more RA claims in the year before diagnosis, as did 1.8% of those with prostate cancer, 2.6% of those with colorectal cancer, and 3.6% of those with lung cancer. Median survival for those without vs. those with RA was 9.5 vs. 7.1 years for breast cancer (P<0.0001), 9.8 vs. 7.3 years for prostate cancer (P=0.001), 3.8 vs. 2.8 years for colorectal cancer (P=0.0009), and 0.7 vs. 0.9 years for lung cancer (P=0.08).

For all four types of malignancies, factors that were associated with worse survival were African-American race, lower income, being diagnosed at a later stage, and having more comorbidities.

In another analysis of comorbidities, diabetes and chronic obstructive pulmonary disease (COPD), respectively, were associated with worse survival (P<0.001 for all):

- Breast: OR 1.29 (95% CI 1.23 to 1.35) and OR 1.42 (95% CI 1.34 to 1.49)
- Prostate: OR 1.21 (95% CI 1.16 to 1.26) and OR 1.56 (95% CI 1.49 to 1.63)
- Colorectal: OR 1.12 (95% CI 1.08 to 1.16) and OR 1.28 (95% CI 1.22 to 1.33)
- Lung: OR 1.04 (95% CI 1.01 to 1.08, P<0.01) and OR 1.11 (95% CI 1.08 to 1.14)

In addition, cardiovascular disease was linked with worse survival for breast, prostate, and colorectal cancer, but not for lung cancer.

The researchers noted that the cancers were diagnosed later in RA patients, but that their data did not include potentially relevant information on treatments. “For instance, patients with RA may be less likely to receive certain therapies such as radiotherapy because of fear of complications or may discontinue therapy early. Likewise, effects of immunomodulatory agents used to treat RA could also interfere with tumor immunity and possibly result in worse outcomes,” they wrote.

They concluded, “Additional research is needed to identify potentially modifiable determinants of this effect.”

Study limitations included its reliance on administrative data, and the inclusion of patients only from Texas.

MedPage Today, 9 August 2016

Switching from AS to Active Treatment
(Continued from page 1)

had been diagnosed with low-risk prostate cancer between 2004 and 2012 at Kaiser Permanente in Northern CA. They did not receive any treatment within the first year of diagnosis and had at least two years of follow-up.

“Because Kaiser Northern California is a large, integrated health system covering a diverse population, it was possible to independently assess ethnic and economic influences on treatment choices,” said Stephen Van Den Eeden, PhD, co-principal investigator for the study and lead researcher at the Kaiser Permanente Division of Research in Oakland, CA.”

Non-Hispanic black men were slightly more likely to begin active treatment than non-Hispanic white men, independent of their status at the beginning of the study and follow-up clinical measures. Among men who remained on observation, non-Hispanic black men were rebiopsied within 24 months of diagnosis at a slightly lower rate than non-Hispanic white men.

Despite nonclinical factors like race and ethnicity, Gleason score, progression and results of PSA testing were the primary clinical triggers that prompted active treatment in men on AS. While the results were only marginally significant, they suggest that race may be a factor for switching to active treatment even among men on AS. “These results are important as clinicians may be increasingly hesitant to require men to undergo serial rebiopsies due to complications, yet black men are known to have a greater likelihood of prostate cancer progression, which suggests that clinicians should be particularly vigilant in the surveillance of black men on AS,” noted Dr. Kelly.

Commenting on the study, David F. Penson, MD, MPH, of the Department of Urologic Surgery at Vanderbilt University Medical Center and the Veterans Affairs Tennessee Valley Geriatric Research, Education, and Clinical Center, noted that the current study “underscores the need to develop patient navigation tools for prostate cancer that are racially and culturally tailored to individual patients.”

The ASCO Post, 29 July 2016
P1, “Markers that Cause...”
Why do some prostate cancer patients who receive radiotherapy (RT) develop side effects while others do not? Many people may first expect something technical would explain these outcomes. However, it is also possible that there are genetic reasons that predispose some men to have an adverse outcome. Work by West, et al., has, thus far, found two SNP’s that were associated with a greater risk of urinary problems following RT. Much more work is needed but the potential is that in the future, men could be tested for risk factors for this side effect and, if present, they could be advised to select some other form of therapy.

The Bottom Line: A genetic test for genetic factors that predict a greater chance of side effects from RT may one day be possible.

P1, “Sociodemographic...” As interest in Active Surveillance (AS) grows, there is an important need to understand the reasons why men choose it initially and then discontinue it even if their cancer has not changed. As a first step, we need to identify whether there are economic, racial and/or social factors that play a role. The article by Van Den Eeden, et al., looked at a large cohort of men from California and found that African-American men are slightly more likely to go on AS and may stay on it more often. Reasons for that observation are unclear but are worth exploring so that better counseling can occur and the right men will stay on it when appropriate.

The Bottom Line: Factors other than characteristics about the cancer may explain why some men choose AS and decide to come out of it despite no change in their cancer. More work is needed in this area.

P1, “Salvage Radiotherapy...” When is the best time to administer salvage RT (SRT) after RP? Over the years, results from uncontrolled studies suggested that giving SRT to men with a lower PSA is better, but data from one large randomized study showed that the benefit was quite small. A new, but also uncontrolled study from Stish and co-workers reported results in men receiving SRT using a multivariable analysis. The research found that a higher proportion of men given SRT when PSA levels were above 0.5 ng/mL developed metastases and had a lower prostate cancer survival compared to men treated when PSA levels were lower. However, they did not find an impact on overall survival. A number of reasons could explain these findings; however, the real question is whether they proved that SRT given before PSA rises above 0.5 ng/mL is truly beneficial. Unfortunately, uncertainty remains.

The Bottom Line: More data are needed to determine whether initiating salvage RT before the PSA exceeds 0.5 ng/mL truly benefits men.

P2, “RALP vs. RRP...” Since the development of robotic laparoscopic radical prostatectomy (RARP), surgeons have had a long-standing debate about whether it is a better surgical method than the traditional open retropubic RP (RRP). Finally, a properly designed randomized study is in progress with some early results now available. Yaxley and co-workers randomized 308 men to one of these methods and using validated surveys, they found no significant difference in urinary and sexual function at six and 12 weeks post surgery between the two surgical methods. A slightly higher rate of intra-operative and post-operative complications was seen for the RRP group. One weakness of the study is that 18% of the enrolled patients did not complete the survey, which could introduce some bias. Nevertheless, the authors deserve credit for conducting this important trial.

The Bottom Line: Based on a randomized study, urinary function and sexual function at six and 12 weeks did not differ significantly between open and robotic RP.

P3, “Olanzapine (Zyprexa®)...” One of the debilitating side effects of chemotherapy is nausea and vomiting. The randomized study by Navari, et al., compared olanzapine or placebo in men receiving chemotherapy with standard nausea prophylaxis and found a very significant reduction in nausea and vomiting at three time periods; in the first 24 hours after chemotherapy, at 24-120 hours and for the entire time. The study did not test men with prostate cancer, but these same side effects are associated with docetaxel so it is possible that prostate cancer patients could also benefit. New studies are clearly needed.

P5, “Brouhaha About...” Politicians aren’t the only ones criticizing the media these days, doctors do too. That has been the upshot of an article questioning whether decreased screening is resulting in an increase in metastatic prostate cancer as suggested by an article from Weiner and co-workers. They looked at the annual number of metastatic cases in the national cancer database and reported that during 2004-2013 there was a marked increase. As the article in the Hot SHEET points out, numbers do not provide an accurate look at whether new trends are occurring. That can only be determined by looking at the rate over time. Other important facts include the following: (1) a look at the SEER data shows that during that same period, the annual death rate from prostate cancer declined by about 3.5% each year. That goes against the suggestion by the authors that the disease is worsening. (2) There was no real change in the percentage of high-risk cancers at the beginning and end of the time period. (3) Lastly, the change in the guideline from the US Public Task Force did not occur until 2012, so that could not possibly explain why the absolute number of cases might have changed years before that.

The Bottom Line: This study does not prove that either the disease is worsening or that screening is resulting in more metastatic disease.
Salvage RT Post-RP (Continued from page 2)

of SRT can be further augmented with dose escalation and ADT,” Dr. Stish said. “These data, in conjunction with the previously published ASTRO/AUA Consensus Guidelines, provide clear evidence that men with detectable PSA after surgery need to be counseled about the strong benefits of SRT to the prostate fossa when PSA becomes detectable,” he added.

“While the decision to proceed with SRT should be made as a part of a shared decision-making process between clinician and patient, these data provide strong evidence against prolonged monitoring of detectable PSA without discussion of the potential risks of deferring or omitting SRT,” Dr. Stish concluded.

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Zypraxa Prevents CIN (Continued from page 3)

a matching placebo daily on days one through four. Nausea prevention was the primary endpoint, with a complete response of no emesis and no need for use of rescue medication being the secondary endpoint. The complete-response rate was also significantly increased with olanzapine during all three periods: 86% versus 65%, 67% versus 52%, and 64% versus 41%, respectively.

The authors noted that other phase III research has reported similar benefits with olanzapine for controlling chemotherapy-induced nausea and emesis. Although no grade 5 toxic effects were observed, some olanzapine recipients experienced greater sedation – rated as severe in 5% of patients – on day two. This symptom generally abated on days three, four, and five despite continued administration of oral olanzapine on days three and four, “suggesting that patients adapted to the drug’s sedative effect,” Navari and associates wrote.

There was no olanzapine-related increase in appetite, no serious adverse events, and no discontinuations due to toxic effects. “In view of the temporary drowsiness reported in this trial and previous reports, more detailed information on drowsiness ratings, as well as the use of a lower dose of olanzapine (5 mg), could be explored in future trials.”

A limitation of the study is that it evaluated only a single 10-mg dose level of olanzapine, although lower or higher doses might impact efficacy, toxicity, or both. In addition, the study did not address the efficacy of olanzapine for multiple chemotherapy cycles. “These issues should be considered in future clinical trials,” the researchers wrote.

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