MRI-Ultrasound Fusion Prostate Biopsy Find More High-Grade, Fewer Low-Grade Tumors

Targeted prostate biopsies that fuse magnetic resonance imaging (MRI) and ultrasound detect more high-grade and fewer low-grade prostate tumors compared with traditional systematic 12-core biopsy (SB), results of a new study confirm. The study also suggests that multiparametric MRI (mp-MRI) performed before biopsy can predict the risk of high-grade cancer.

Increasing evidence supports using mp-MRI-ultrasound fusion-targeted prostate biopsy (MRF-TB) in place of the SB to improve detection of clinically significant prostate cancer while limiting detection of low-risk cancers, Dr. Samir Taneja and colleagues from New York University Langone Medical Center noted online in the journal *European Urology*.

They compared MRF-TB and SB results and studied the relationship between biopsy outcomes and prebiopsy MRI in 601 consecutive men presenting to their center for prostate biopsy over a 26-month periods. All of the men were offered an MRI before biopsy and were assigned a maximum MRI suspicion score (mSS). Those with an abnormal MRI underwent compared MRF-TB and SB results and studied the relationship between biopsy outcomes and prebiopsy MRI in 601 consecutive men presenting to their center for prostate biopsy over a 26-month periods. All of the men were offered an MRI before biopsy and were assigned a maximum MRI suspicion score (mSS). Those with an abnormal MRI underwent MRF-TB and SB. Of the 601 men, 292 (48%) had no prior biopsy, 172 (29%) had a prior negative biopsy, and 137 (23%) had prior cancer.

For detecting all prostate cancers, MRF-TB was on par with SB (p=0.731). However, MRF-TB detected significantly fewer Gleason score (GS) 6 tumors (75 vs. 121; p <0.001) and significantly more GS 7 or higher cancers (158 vs. 117; p <0.001). A (Continued on page 3)
Differential Post-Prostatectomy Cancer-Specific Survival of Occult T3 Vs. Clinical T3 Prostate Cancer: Implications for Managing Patients Upstaged on Prostate Magnetic Resonance Imaging

Muralidhar V, Dinh KT, Mahal BA, et al

Urol Oncol 2015; 33(7): 330.e19-25

Purpose/Objective: Long-term androgen deprivation therapy (ADT) was proven in randomized trials to be superior to short-term ADT for radiation-managed men who have clinical T3 (cT3) disease, but it is unknown whether men with T3 disease seen only on magnetic resonance imaging (MRI) require similarly aggressive treatment. We attempted to study this issue by analogy to comparing long-term post-prostatectomy (RP) survival of men with cT3 disease vs. cT1/T2 disease upstaged to pathologic T3 disease.

Methods: The Surveillance, Epidemiology, and End Results (SEER) database was used to identify 60,165 men diagnosed with prostate adenocarcinoma between 1995 and 2002 who underwent RP. Prostate cancer-specific mortality (PCSM) was evaluated at stage adjusting for grade, marital status, race, sex, year of diagnosis, and age.

Results: The median follow-up was 10.5 years. Men with cT1/T2 but pathologic T3a disease had significantly better 10-year PCSM than men with cT3 disease had (3.0% vs. 9.9%, adjusted hazard ratio [AHR] = 0.420, P< 0.001), but they had worse PCSM than men with pathologic T2 disease had (3.0% vs. 9.1%, AHR = 2.53, P< 0.001). Of men with occult T3a disease, those with low-grade/intermediate-grade disease (Gleason score 7 or less) had a slightly higher 10-year PCSM when compared with those with pathologic T2 disease (1.3% vs. 0.91%, AHR = 1.69, P< 0.001). Men with cT1/T2 and pathologic T3b disease had similar PCSM as men presenting with cT3 disease (11.0% vs. 9.86%, AHR = 1.14 [0.862, 1.52], P = 0.353).

Conclusions: Men with occult T3a disease had less than half the risk of PCSM as those with cT3 disease, and a subset of those men had similar risk as patients with pathologic T2 disease. Therefore, it is possible that radiation-managed patients with low-grade/intermediate-grade T3a disease by MRI alone might not require long-term ADT. However, men with occult T3b or high-grade occult T3a disease have similar PCSM as those presenting with cT3 disease, so they should be treated as aggressively, including long-course ADT when managed by radiation.

Efficacy and Safety of Abiraterone Acetate in Elderly (≥75 Years) Chemotherapy-Naive Patients with Metastatic Castration-Resistant Prostate Cancer

Smith MR, Rathkopf DE, Mulders PF, et al

J Urol 4 July 2015; Epub

Purpose: Metastatic castration-resistant prostate cancer (mCRPC) primarily affects elderly men. In this post hoc analysis we investigated the safety and efficacy of abiraterone acetate (AA) in elderly (≥75 years) and younger (<75 years) patients. Subgroups at the prespecified interim analysis (55% of total overall survival [OS] events) for the COU-AA-302 trial.

Materials and Methods: Men were stratified and randomized 1:1 to AA 1,000 mg plus prednisone or prednisolone 5 mg twice daily (AA-prednisone) vs. placebo plus prednisone or prednisolone 5 mg twice daily (prednisone alone). Co-primary end points were radiographic progression-free survival (rPFS) and OS. Median time to event and hazard ratio (HR) were estimated using Kaplan-Meier method and Cox model, respectively.

Results: Elderly men (n=350) treated with AA-prednisone had significant improvements in OS and rPFS vs. prednisone alone (HR 0.71 [95% CI 0.53-0.96] and HR 0.63 [95% CI 0.48-0.83], respectively), similar to younger men (n=738, HR 0.81 [95% CI 0.63-1.03] and HR 0.49 [95% CI 0.40-0.59], respectively). All secondary end points favored the AA-prednisone arm for both age subgroups. Specific adverse events with AA-prednisone were similar between age subgroups. Elderly men in both treatment arms had higher rates of fluid retention and cardiac disorders than younger patients, although rates of dose reduction or treatment interruptions due to adverse events were low in both age subgroups.

Conclusions: AA demonstrated clinical benefit and was well tolerated in both elderly and younger men with chemotherapy-naive mCRPC, thus supporting it as a treatment option for elderly men who may not tolerate other therapies with greater toxicity.
Doc Moyad’s What Works & What is Worthless Column, Also Known as “No Bogus Science” Column –

“There are more obese individuals than overweight individuals for the first time in US history!”
Mark A. Moyad, MD, MPH, Univ. of Michigan Medical Center, Department of Urology

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

Bottom Line:
The obesity epidemic is now a super-epidemic! There are more obese individuals than overweight individuals for the first time in US history! New U.S. statistics shows nearly two-thirds (66%) of adults are now at an unhealthy weight!1 YIKES!!!

It seemed so easy when I was a kid. Play for 30 minutes before school, and then 45 minutes of gym (aka “PE”) class daily, Lunch and then recess and play for another 30 minutes, and then play with my buddies some kind of sport after school for at least another 60 minutes (30+45+30+60=165 minutes, or > 2.5 hours of minimum playing time per day!!!) and bam I was the amazing deflated kid (like most of the other kids)! I was skinnier than any world champion marathon runner or mosquito on a diet. In fact, the heavy kid in school was such an oddity that other kids called that person “the heavy kid” (not plural but singular). Today, the heavy and skinny kids are now the heavy adult majority. This new scary data was derived from the National Health and Nutrition Examination Survey or NHANES (conducted by CDC). Approximately 75% of men (40% overweight + 35% obese) and 67% of women (30% overweight + 37% obese) ages 25 and older are currently overweight or obese versus 20 years ago when it was 63% of men and 55% of women. Currently, there are 2.5 million more obese vs. overweight individuals in the US. People ask me about supplements and prescription pills all the time for everything from sexual dysfunction, incontinence, fatty liver, low testosterone, high cholesterol, blood pressure, blood sugar... you name it and I have heard it. Yet, right in front of us is the ultimate lifelong challenge (really solution) of how do I achieve a healthy weight? If this goal is ever achieved by most Americans I cannot begin to tell you just how bored many doctors in the US would be simply because most of our health pills are riding the heels of the obesity epidemic and business is booming! Whatever it takes to help you lose weight/waist please do it now, because the bottom line is that we have hit the bottom line and almost every health condition ever discussed in this newsletter gets worse with weight gain! Ahh, the secret to life revealed by Moyad once again (and you thought the secret to life was more beer and pizza...that use to be the secret until this new paper was published and now it is part of the culprit)!

Reference:

Phosphodiesterase Type 5 Inhibitors for Erectile Dysfunction Associated With Risk of Melanoma

In a study in Swedish men reported in JAMA, Loeb et al found a statistically significant increased risk of melanoma in those using oral phosphodiesterase type 5 inhibitors (PDE5-i) for erectile dysfunction. However, risk was not significantly elevated in men filling multiple PDE5-inhibitor prescriptions. The target of these drugs is part of the RAS-RAF-MEK-ERK signaling pathway involved in the development of melanoma. The nationwide population-based, nested case-control study involved data from the Swedish Prescribed Drug Register, Swedish Melanoma Register, and other Swedish health-care registers and demographic databases. The study included 4,065 melanoma cases diagnosed between 2006 and 2012 and 5 randomly selected controls per case matched for year of birth. Analysis of PDE5-i use was according to use of sildenafil (Viagra) or use of vardenafil or tadalafil (Cialis).

In total, 435 men with melanoma (11%) had filled prescriptions for PDE5-Is; of these, 275 (63%) had filled prescriptions for sildenafil and 224 (51%) had filled prescriptions for vardenafil or tadalafil. Among 20,325 controls, 1,713 (8%) had filled prescriptions for PDE5-Is. In multivariate analysis, use of PDE5-Is was associated with increased risk for melanoma (odds ratio [OR] =1.21, 95% confidence interval [CI] = 1.08-1.36). Risk was significantly increased among men who had filled a single prescription (4% for cases vs 3% for controls, OR = 1.32, 95% CI = 1.10-1.59), but was non-significantly increased among

Magnetic Resonance Imaging-Ultrasound Fusion Biopsy (Continued from page 1)

higher mSS correlated strongly with a greater odds of finding GS 7 or higher cancer (p <0.001).

Compared to SB, MRF-TB found more GS 7 or higher tumors in men with no prior biopsy (88 vs. 72; p = 0.012), in men with a prior negative biopsy (28 vs. 16; p = 0.010), and in men with a prior diagnosis of cancer (42 vs. 29; p = 0.043). MRF-TB detected fewer GS 6 tumors in men with no prior biopsy (32 vs. 60; p<0.001) and in men with prior cancer diagnosis (30 vs. 46; p = 0.034).

“These findings suggest that prebiopsy mp-MRI and MRF-TB should be considered for all men undergoing prostate biopsy. In addition, mSS in conjunction with biopsy indications may ultimately help in identifying men at low risk of high-grade cancer for whom prostate biopsy may not be warranted,” they conclude.

Authors of an opinion piece published journal issue caution that despite “accumulating evidence” favoring mp-MRI-targeted prostate biopsy (PB), “there are still some open questions and concerns,” which they describe in detail in their article.

As it stands, “we believe further scrutiny is warranted before large-scale dissemination of MRI-informed PB takes place. If we had to foresee a major change in PB practice, this would be one in which PB strategy would be personalized according to several determinants, thus establishing the concept of individualized precision biopsy,” conclude Dr. Gianluca Giannarini and colleagues from the Urology Unit, Academic Medical Centre Hospital Santa Maria della Misericordia, Udine, Italy.

*Reuters Health, 6 July 2015*
states. All but three practices are community based, and the practices are both large and small in size.

All of the 10,472 men included in the study had localized disease (clinical stage T3a or lower with no nodal or distant metastases) and were managed with prostatectomy, radiation, ADT, or AS. The men had low-, intermediate-, or high-risk disease (determined on the basis of CAPRA scores).

The authors found that AS use for low-risk disease (CAPRA 0-2) “remained low” from 1990-2009 (ranging from 6.7% to 14.3%) but then dramatically spiked to 40.4% in 2010-2013 (P < 0.001 for trend). During this time frame, the inappropriate use of ADT dropped in men with intermediate-risk (from 9.7% in 1990 to 3.8% in 2010-2013) and high-risk disease (from 29.8% in 1990 to 50% in 2005-2009 and then back down to 24% in 2010-2013).

The authors explain that potential curative local treatment should be used in these men at higher risk, rather than a systemic monotherapy. But, as widely reported, there were ongoing financial incentives for clinicians to prescribe ADT before Medicare reform occurred in 2005.

“It is reassuring to see this evidence that AS is finally being embraced in the United States,” said Stacy Loeb, MD, from New York University, in New York City, who was not involved in this research and was asked for comment.

She also said that the CapSURE data agree with an American registry study from the state of Michigan that reported that 49% of eligible men received AS.

**Adding Biopsy Factors to PRIAS Criteria May Help Predict Unfavorable Prostate Cancer**

Adding biopsy factors to existing Prostate Cancer Research International: Active Surveillance (PRIAS) criteria may boost the ability to detect prostate cancer that is unfavorable for active surveillance (AS), researchers from Italy report. “The risk of misclassifying men on AS based on PRIAS criteria is 26%,” Dr. Giorgio Ivan Russo from the University of Catania stated. “We proposed to incorporate biopsy features in order to reduce that risk.”

The PRIAS criteria include clinical stage T1c or T2 disease, PSA ≤10 ng/mL, Gleason score ≤6, PSA density <0.2 ng/mL, and one or two positive biopsy cores.

Dr. Russo’s team assessed performance of biopsy factors when added to the PRIAS criteria in 143 men who underwent radical prostatectomy but were eligible for AS. Two-thirds of these men had favorable disease and one-third had unfavorable disease, researchers report online in Prostate Cancer and Prostatic Disease, June 2.

On multivariate analysis, inclusion of maximum cancer length, cumulative cancer length, cumulative length and cancer involvement of positive cores significantly increased the accuracy of the model in predicting unfavorable disease.

“Our findings suggest that models including biopsy factors could not only predict unfavorable disease in men eligible for AS but could also minimize the risk of missing high-grade and non-organ-confined cancers,” researchers say. “The model cannot replace the entire PRIAS frame, the inappropriate use for low-risk disease (CAPRA 0-2) “remained low” from 1990-2009 (ranging from 6.7% to 14.3%) but then dramatically spiked to 40.4% in 2010-2013 (P < 0.001 for trend). During this time frame, the inappropriate use of ADT dropped in men with intermediate-risk (from 9.7% in 1990 to 3.8% in 2010-2013) and high-risk disease (from 29.8% in 1990 to 50% in 2005-2009 and then back down to 24% in 2010-2013).

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Medscape Medical News
7 July 2015

(Continued on page 5)
Prostate Cancer Education, Detection, and Follow-Up in a Community-Based Multiethnic Cohort of Medically Underserved Men

Ashorobi OS, Frost J, Wang X, et al
Am J Mens Health 18 May 2015 pii: 1557988315584794

The Prostate Outreach Project (POP) provided free prostate cancer (PCa) education and early detection to medically underserved communities. POP recruited participants in medically underserved communities. PCa education and detection events occurred in POP locations (static or natural gathering places) within the community. PCa education was delivered by video and evaluated using a questionnaire. Screening consisted of serum prostate-specific antigen and digital rectal examination. A navigated follow-up strategy was utilized to provide medical care for participants with abnormal screening examinations (ASE). POP recruited 4,420 men, 62.8% (2,667) of whom were African American (AA). Most participants had a high school education and no prior screening. Fifty-four percent (2,159) were uninsured and 41% (1,811) had no access to a physician. PCa knowledge increased following the educational video. Prostate-specific antigen levels were elevated in 9.8% (436), while 6.9% (233) had an abnormal digital rectal examination. Follow-up among 609 men with ASE was successful in 40% (244), despite a navigated approach. Overall, 3.3% (144) cancers were diagnosed among the POP with AA participants exhibiting a significantly higher incidence.

Recruitment, education, and PCa testing among a medically underserved cohort was successful. However, failure to follow through on ASE could contribute to maintaining the disparity in PCa outcomes noted among AAs and the medically underserved if not addressed.

DNA Repair Kinase Identified as Key Driver of Metastasis in Prostate Cancer

Researchers at Thomas Jefferson University reported finding a single molecule that appears to be the central regulator driving metastasis in prostate cancer. The study, published by Goodwin et al in Cancer Cell, offers a target for the development of a drug that could prevent metastasis in prostate cancer and possibly other cancers as well.

“Finding a way to halt or prevent cancer metastasis has proven elusive. We discovered that a molecule called DNA-PKcs could give us a means of knocking out major pathways that control metastasis before it begins,” said Karen Knudsen, PhD, Director of the Sidney Kimmel Cancer Center at Thomas Jefferson University; the Hilary Koprowski Professor and Chair of Cancer Biology; and Professor of Urology, Radiation Oncology, and Medical Oncology at Jefferson.

Dr. Knudsen and colleagues have shown that one molecule appears to be central to many of the processes required for a cancer to spread. That molecule is a DNA repair kinase called DNA-PKcs. The kinase rejoins broken or mutated DNA strands in a cancer cell, keeping alive a cell that should normally self-destruct. In fact, previous studies had shown that DNA-PKcs was linked to treatment resistance in prostate cancer, in part because it would repair the usually lethal damage to tumors.

(Continued on page 6)

Early ADT for Recurrent Prostate Cancer May Hike Death Risk

Early androgen deprivation therapy (ADT) may increase the risk of death among men who receive it after experiencing biochemical recurrence (BCR) of prostate cancer following radical prostatectomy, according to study data presented at the 2015 American Urological Association annual meeting.

This adverse effect appears to be limited to men younger than 65 years when they experience BCR and those with low-risk disease, reported a research team led by Stephen J. Freedland, MD, of Cedars-Sinai Medical Center in Los Angeles.

Dr. Freedland and his colleagues retrospectively analyzed data from 468 patients who experienced BCR after RP. The median follow-up after BCR was 70 months. Of the 135 men who received early ADT (defined as receipt of ADT when PSA levels were less than 5 ng/ml), 42 died.

In adjusted analyses, early ADT was associated with a significant 68% increased risk of death compared with the 333 men who received conventional therapy (no ADT or ADT started when PSA levels were 5 ng/mL or higher).

Finally, data suggest that men with a PSA doubling time of less than 9 months fared better with early ADT, whereas those with longer PSA doubling times fared worse.

In a poster presentation, Dr. Freedland’s team concluded that the “risks and benefits of ADT must be weighed and taken into account when deciding timing of treatment.” Whether the harmful effect of early ADT is due to true harm, treatment bias, or unmeasured confounding is not known, they noted.

Dr. Freedland told Renal & Urology News, “These data support other recent data that ADT can come with a price, and is not appropriate for all men and should be used selectively for those men at the highest risk of death from prostate cancer.”

Renal and Urology News June-July 2015

Biopsy Features and PRIAS (Continued from page 4) model,” Dr. Russo said. “However, urologists involved in PRIAS protocol can take into account that biopsy features significantly improve its accuracy.”

Dr. Marc Dall’Era from the University of California, Davis, stated, “Although adding these findings will help identify men with extremely low-risk prostate cancer, I am concerned that if we were to include such stringent criteria, we will further limit the number of men eligible for AS. Since there is no evidence that the primary outcome measure of this study correlates with long-term outcomes such as disease progression over time or prostate cancer specific mortality, these criteria should not be generalized across the board.”

Reuters Health, 7 July 2015

PROSTATE CANCER HELPLINE: 1-800-808-7866 WWW.USTOO.ORG
caused by radiation therapy and other treatments.

The researchers showed that DNA-PKcs also appears to act as a master regulator of signaling networks that turn on the entire program of metastatic processes. Specifically, DNA-PKcs modulates the Rho/Rac enzyme, which allows many cancer cell types to become mobile, as well as a number of other gene networks involved in other steps in the metastatic cascade, such as cell migration and invasion.

In addition to experiments in prostate cancer cell lines, Dr. Knudsen and colleagues also showed that in mice carrying human models of prostate cancer, the development of metastases could be blocked by using agents that suppress DNA-PKcs production or function. In mice with aggressive human tumors, an inhibitor of DNA-PKcs reduced overall tumor burden in metastatic sites.

In a final analysis that demonstrated the importance of DNA-PKcs in human disease, the researchers analyzed 232 samples from patients with prostate cancer for the amount of DNA-PKcs those cells contained and compared those levels with the patients’ medical records. They saw that a spike in the kinase levels was a strong predictor of developing metastases and poorer outcomes in patients with prostate cancer. They also showed that DNA-PKcs was much more active in human samples of castrate-resistant prostate cancer, an aggressive and treatment-resistant form of the disease.

“These results strongly suggest that DNA-PKcs is a master regulator of pathways and signals that lead to the development of metastases in prostate cancer and that high levels of DNA-PKcs could predict which early stage tumors may go on to metastasize,” said Dr. Knudsen.

A phase I trial studying a drug developed to inhibit DNA-PKcs is underway (NCT01353625). “We are enthusiastic about the next step of clinical assessment for testing DNA-PKcs inhibitors in the clinic. This new trial will be for patients advancing on standard-of-care therapies and will be available at multiple centers connected through the Prostate Cancer Clinical Trials Consortium, of which we are a member,” explained Dr. Knudsen.

“Although the pathway to drug approval can take many years, this new trial will provide some insight into the effect of DNAPKcs inhibitors as antitumor agents. In parallel, using this kinase as a marker of severe disease may also help identify patients whose tumors will develop into aggressive metastatic disease, so that we can treat them with more aggressive therapy earlier,” said Dr. Knudsen.

“Given the role of DNA-PKcs in DNA repair as well as control of tumor metastasis, there will be challenges in clinical implementation, but this discovery unveils new opportunities for preventing or treating advanced disease.”

Dr. Knudsen is the corresponding author of the Cancer Cell article. The ASCO Post, 15 July 2015

Can Asthma Protect Men From Lethal Prostate Cancer?

Men with asthma are less likely to have aggressive prostate cancer or to die from the disease, according to a large, prospective cohort study published in the International Journal of Cancer.

The findings surprised investigators, who thought that immune system characteristics of asthma might be associated with worse cancer outcomes.

Lead investigator Elizabeth Platz, ScD, an epidemiologist at Johns Hopkins University, and colleagues analyzed data from the Health Professionals Follow-Up Study, an ongoing prospective cohort of approximately 50,000 men ages 40 to 75 at enrollment in 1986. Participants completed questionnaires on demographics, medical history, and lifestyle factors at regular yearly intervals.

Data from 1986–2012, was examined, excluding men with any cancer diagnosis at baseline. For men reporting a prostate cancer diagnosis, investigators checked medical records and pathology reports. A total of 6,294 cases of incident prostate cancer were confirmed. Of these, 798 were classified as “lethal” (diagnosed with distant metastases or progression to distant metastases). Of these cases, 625 men actually died from the disease.

At baseline, 2,516 men (5.3%) had a history of asthma, and an additional 1,906 men were diagnosed with asthma during follow-up. Cox proportional hazards regression was used to estimate relative risks, adjusting for known prostate cancer risk factors such as age, race, BMI, and smoking. Key results included the following:

Men with a diagnosis of asthma at any time during the study were less likely to develop lethal prostate cancer (RR 0.71; 95% CI 0.51-1.00). Similarly, these men were also less likely to die from prostate cancer (RR 0.64; 95% CI 0.42-0.96).

A history of asthma was weakly associated with reduced risk for any kind of prostate cancer (RR 0.89; 95% CI 0.78-1.00).

Men with a relatively recent diagnosis of asthma (within the past 30 years) were at even lower risk for lethal prostate cancer (RR 0.36; 95% CI 0.14-0.97) than men who had been diagnosed more than 30 years ago (RR 0.81; 95% CI 0.52-1.24).

Researchers considered several possible explanations. One is a TH2-skewed immune response linked with asthma, which also results in large numbers of circulating eosinophil cells. These cells are believed to play an important role in antitumor immune response, and have in fact been shown to lyse prostate cancer cells in vitro.

Another possibility is TH17 T cells, which have been associated with chronic inflammation and cancer in both human and animal studies. Men with asthma might have a genetic or environmental propensity for a CD4+ T-cell helper response skewed away from a TH17 response.

(Continued on page 8)
a1p1c1 A growing controversy surrounds whether to routinely use mp-MRI and MRI-US fusion biopsy to evaluate men for prostate cancer in place of random core ultrasound-guided biopsies. The advantage of using MRI appears to be a significantly greater likelihood of finding Gleason 7 or higher cancer and a significantly lower chance of finding Gleason 6 cancer. It is important to separate the controversy into a discussion of whether it is the first biopsy, a biopsy after cancer is confirmed, or after a negative biopsy. The article by Taneja, et al looked at over 600 men undergoing biopsy by both methods and confirmed the above findings. However, the accompanying editorial still raises questions about its role. Regardless of when it is used, it will be more expensive and inconvenient, requiring men to undergo two procedures instead of just one. As for doing it to evaluate men undergoing their first biopsy, there is a controversy. Although it certainly enables men to avoid a decision about whether to treat or observe a Gleason 6 cancer, failure to make that diagnosis may not be what men want. Also, we know that not all Gleason 6 cancers are safe to observe. Therefore if a man has Gleason 6 cancer but it is not diagnosed, will he file a lawsuit years later if his cancer was missed using MRI? A better case may be made for follow-up biopsy if a man is on AS because one factor he will consider is whether his Gleason score increases to 7. Currently, doctors are also using an increase in tumor volume, even of Gleason 6 to recommend definitive therapy. Although it may or may not be a valid decision, more data are needed to know if that is true. Until then, it is another weakness of MRI guided biopsy. For now, more information is still needed to determine the best approach.

The Bottom Line: mp MRI fusion biopsy has advantages and disadvantages and more data are needed to know its exact role.

a3p1c3 As the adoption of active surveillance (AS) gradually increases, the optimal time to undergo definitive therapy becomes the critical question. One can readily understand the doctor’s reluctance to delay therapy if the PSA, the tumor grade, or the amount of cancer on biopsy increases. As experience grows and more data become available, doctors may become more comfortable with conservative therapy in the face of those changes. The study by Welty and co-workers adds some new information about the pathological findings in the face of an increase in tumor grade on a repeat biopsy. They found that about one-third of the patients had a drop in the final grade compared to the previous biopsy, meaning that not all tumor grade increases seen on biopsy are real. Only 6% had a further increase in tumor grade. What does this mean? Unfortunately, the answer is not entirely clear. The fact that the tumor grade was over read does not tell us what should be done when an increase in tumor grade is observed. These data tell us nothing about the long-term implications of delaying treatment until the tumor grade increases or not treating a patient when tumor grade increases. For now, we clearly need more information to help guide patients, but this study does not really help make that decision.

The Bottom Line: More data are needed to know the best approach to deciding when to abandon AS.

a4p2c2 The study by Muralidhar, et al attempts to use SEER data from RP to make suggestions for men undergoing radiotherapy (RT) who might benefit from ADT. They observed better prostate cancer specific survival in men with occult pathologic stage T3 disease vs. clinical T3 disease in a non-random assessment of men treated between 1995 and 2002. On the basis of their findings they make suggestions regarding the use of ADT in men undergoing RT for T3 disease. Unfortunately, there is no way to know if that is appropriate. Extrapolating findings from one set of data accumulated in a non-randomized fashion to another clinical situation is not appropriate. We cannot know the impact of that approach unless a properly done study is performed.

The Bottom Line: Using data from a surgical cohort to make suggestions about how to manage men undergoing RT is filled with possible biases and inaccuracy.

a5p2c2 Abiraterone acetate has been a definite benefit for men with castrate-resistant prostate cancer both before and after docetaxel chemotherapy. As with all drugs, however, there are some potential risks from side effects. The report by Smith, et al looked at the impact of patient age on outcomes. Men over 75 had a slightly better survival compared to men under 75, but also had a higher incidence of fluid retention and cardiac disorders. Despite those rates, however, older men were no more likely to require a dose adjustment. The good news for older men is that they can benefit from this therapy with little risk.

The Bottom Line: Abiraterone acetate appears well tolerated in men over 75. Despite the higher incidence of side effects, the drug can be offered with careful monitoring.

a8p5c1 Are men with little or no insurance able to make an informed decision about managing their prostate cancer? Ashorobi, et al conducted an education program in an underserved population of men and then provided screening where appropriate. They found, as others have, that education may improve awareness. However, only 40% of the men underwent evaluation for a suspected cancer underwent follow-up. Although the program provided support to help men get their diagnosis, it is unclear how treatment is funded. We do not know the reasons why men did not seek follow-up, but clearly for a program to be successful, it must be able to eliminate all obstacles for complete care.

The Bottom Line: Education programs can improve awareness of economically disadvantaged men, however, that does not insure that appropriate follow-up will occur and more information is needed to understand the reasons and make changes.

a10p5c3 The pendulum is shifting on the use of andro- (Continued on page 8)
Melanoma
(Continued from page 3)

those who filled two to five prescriptions (4% vs 3%, OR = 1.14, 95% CI = 0.95-1.37) or among those who filled six or more prescriptions (3% vs 2%, OR = 1.17, 95% CI = 0.95-1.44). Risk estimates were similar for sildenafil use and vardenafil or tadalafl use.

PDE5-I use was significantly associated with melanoma stage 0 (OR 1.49, 95% CI 1.22-1.83) and stage I (OR 1.21, 95% CI 1.02-1.43), but not stage II through IV (OR 0.83, 95% CI 0.63-1.09).

Investigators concluded: “In a Swedish cohort of men, the use of PDE5-Is was associated with a modest but statistically significant increased risk of malignant melanoma. However, the pattern of association (e.g., the lack of association with multiple filled prescriptions) raises questions about whether this association is causal.”

The ASCO Post, 7 July 2015

Asthma
(Continued from page 6)

Finally, CD4+ helper T cells may offer an explanation. These cells are thought to limit host antitumor response, and research suggests they are deficient either in function or number in asthma.

“Although at this time we do not have an explanation for the difference in the direction of the associations for asthma and hay fever with prostate cancer, our findings may lead to testable hypotheses about specific immune profiles in the etiology of lethal prostate cancer and the disease overall,” the investigator concluded.

Neil Schachter, MD, a pulmonologist at Mount Sinai Hospital, in New York, noted “It’s an interesting association, but I suspect it’s more a question of several degrees of separation rather than a more direct association.”

MedPage Today
18 May 2015

Dr. Chodak’s Bottom Line
(Continued from page 3)

gen deprivation therapy (ADT) for men with a biochemical recurrence after radical prostatectomy (RP). For years the thinking was earlier was better, however, as the long-term side effects became increasingly recognized, that belief has changed. The study by Freedland, et al, offers some additional data about the potential consequences, although their findings are hard to accept. Treating men under age 65 with a PSA less than 5 ng/mL resulted in a significantly higher risk of mortality compared to not using ADT or using it when the PSA was above 5 ng/mL, however, the opposite was true for men over age 65. This finding is hard to understand. What is so special about age 65 or a PSA of 5 ng/mL to account for different outcomes? The question is whether the findings are valid. As I have said so many times before, this is not a prospective randomized trial and therefore the findings may be very misleading. The authors’ recommendation about accepting that early ADT is a trade-off of risks and benefits is definitely valid, but we need much better information before being able to decide the timing of that therapy. One could make a good argument, however, that men should not undergo early ADT for a rising PSA of any level until we have proof from a randomized study that it improves survival.

The Bottom Line: Randomized data are needed to know the optimal timing of ADT for a rising PSA after RP.

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