Hot SHEET
Us TOO INTERNATIONAL Prostate Cancer Education and Support Network

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After New USPSTF Guidelines Issued, the US Sees a Sharp Decline in Prostate Cancer Screenings – and Diagnoses

The rate of prostate screenings and the incidence of prostate cancer diagnoses have both declined sharply since an expert panel issued controversial recommendations that men should no longer have the simple blood test that can reveal the disease, researchers reported.

The US Preventive Services Task Force concluded in 2012 that the PSA test causes more harm than good, saving few lives but prompting unnecessary surgery, radiation and side effects among men who would never die from the often slow-growing cancer. Except for those with high risk for the disease, men should avoid the blood test, the panel said.

Four years earlier, it had issued similar guidelines for men older than 75. Together, the recommendations countered two decades of medical practice. The result has been a clear decline in the number of men being tested and the discovery of cases of prostate cancer, researchers reported in the *Journal of the American Medical Association*.

Otis Brawley, chief medical officer for the American Cancer Society and an author of the new study, said the decline is a positive sign if it means that more doctors and patients are discussing the pros and cons of the screening and making decisions together.

"It's only a good thing if [the numbers] went down because doctors and patients consciously decided together that it shouldn't be done," Brawley said. "I think it's terrible to tell a man he must

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Active Surveillance Underused in Low-Risk Prostate Cancer

Men assigned to watchful waiting (WW)/active surveillance (AS) for low-risk prostate cancer were less likely to have multiple PSA tests and office visits as recommended within the first two years after their diagnosis, compared with men who received more aggressive treatment for their disease, a population-based study has found.

Of 3,656 men with low-risk prostate cancer followed by WW/AS, only 4.5% had at least four PSA tests and attended four office visits and underwent a repeat biopsy within two years as called for in current guidelines, according to Karim Chamie, MD, of the University of California Los Angeles, and colleagues reported in the journal *Cancer*.

"On a population level, we found that less than 5% of men who did not undergo aggressive treatment for prostate cancer were closely followed – defined as having PSA and office visit every six months – and underwent a repeat prostate biopsy," Chamie told MedPage Today in an email.

"In fact those who underwent aggressive treatment were more likely to undergo more intense follow-up than men who were not treated," he added. "So our study suggests that before we advise our patients to pursue AS for their prostate cancer, we should commit to closely monitoring the cancer with a repeat biopsy and more frequent PSA testing and physical exams."

However, Ballentine Carter, MD, of Johns Hopkins University (JHU), told by MedPage Today that his center's experience with

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New Model for Prostate Cancer Screening May Reduce Number of Prostate Biopsies

A new model for prostate cancer screening can significantly reduce the number of unnecessary biopsies and minimize detection of clinically insignificant disease in comparison with the standard screening approach using PSA alone, the Stockholm 3 (STHLM3) study indicates.

"We have shown that a combination of plasma protein biomarkers, genetic polymorphisms, and clinical variables can improve the specificity of prostate cancer screening significantly compared with PSA in men aged 50– 69 years," write the authors, led by Henrik Grönberg, MD, Karolinksa Institute, Stockholm, Sweden. The study was published online November 9th in the journal *Lancet Oncology*.

"Use of the STHLM3 model in structured screening could reduce the number of prostate biopsy samples taken by about a third compared with the use of PSA screening, [and] importantly, this can be achieved without compromising the number of high-risk cancers diagnosed," Dr. Grönberg said.

STHLM3 was a prospective, population-based diagnostic study in which investigators compared the new screening model with the standard PSA test in men between 50 and 69 years of age living in Stockholm, Sweden. Each study participant underwent both screening methods.

The STHLM3 model involves testing for a combination of

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Biochemical Recurrence Risk Factors in Surgically Treated High- and Very High-Risk Prostate Tumors

Aguilera A, Bañuelos B, Díez J

Central European Journal of Urology 26, September 2015; Epub

Introduction: High- and very high-risk prostate cancers are tumors that display great variation in their progression, making their behaviour and consequent prognosis difficult to predict. We analyse preoperative and postoperative risk factors that could influence biochemical recurrence (BCR) of these tumors.

Material and Methods: We carried out univariate and multivariate analyses in an attempt to establish statistically significant preoperative (age, rectal examination, PSA, biopsy Gleason score, uni/bilateral tumor, affected cylinder percentage) and postoperative (pT stage, pN lymph node affectation, Gleason score, positive surgical margins, percentage of tumor affectation, perineural infiltration) risk factors, as well as their relationship with BCR (PSA >0.2 ng/mL).

Results: We analysed 276 patients with high- and very high-risk prostate cancer that were treated with laparoscopic radical prostatectomy (LRP) between 2003–2007, with a mean follow-up of 84 months. Incidence of BCR is 37.3%. Preoperative factors with the greatest impact on recurrence are suspicious rectal exam (OR 2.2) and the bilateralism of the tumor in the biopsy (OR 1.8). Among the postoperative factors, the presence of a LRP positive surgical margins (OR 3. 4) showed the greatest impact, followed by the first grade of the Gleason score (OR 3. 3).

Conclusions: The factor with the greatest influence on BCR when it comes to surgery and high- and very high-risk prostate cancer is the presence of a positive margin, followed by the Gleason score. Preoperative factors (PSA, biopsy Gleason score, rectal examination, number of affected cylinders) offered no guidance concerning the incidence of BCR.

Validation of a Genomic Classifier for Predicting Post-Prostatectomy Recurrence in a Community-Based Healthcare Setting

Glass AG, Leo MC, Haddad Z, et al

J Urol 25 November 2015; Epub

Purpose: To determine the value of Decipher, a genomic classifier, to predict prostate cancer outcomes among patients following radical prostatectomy (RP) in a community health care setting.

Methods: We examined the experience of 224 men treated with RP, 1997-2009, at Kaiser Permanente Northwest, a large prepaid health plan in Portland, Oregon.

Study subjects had aggressive prostate cancer with at least one of the following criteria: pre-operative PSA ≥20 ng/ml, pathologic Gleason score ≥8, stage pT3, or positive surgical margins at RP. The primary endpoint was clinical recurrence or metastasis after surgery evaluated using a time-dependent c-index. Secondary endpoints were biochemical recurrence and salvage treatment failure. We compared the performance of Decipher alone to the widely used Cancer of the Prostate Risk Assessment Postsurgical (CAPRA-S) score and assessed the independent contributions of Decipher, CAPRA-S and their combination for the prediction of recurrence and treatment failure.

Results: Of the 224 patients, 12 (5.4%) experienced clinical recurrence, 68 had biochemical recurrence and 34 failed salvage treatment. At 10 years after RP, the recurrence rate was 2.6% among patients with low Decipher scores but 13.6% among those with high Decipher scores (p=0.02). When the CAPRA-S and Decipher scores were considered together, the discrimination accuracy of the ROC curve was increased by 0.11 over the CAPRA-S score alone (combined c-index = 0.84 at 10 years post-RP) for clinical recurrence.

Conclusion: Decipher improves our ability to predict clinical recurrence in prostate cancer and adds precision to conventional pathological prognostic measures.

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

"PSA screening study strikes again = Fiber & Exercise & Now Coffee!"

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:

Remember my last column? Here we go again! Let's stop arguing about PSA screening and appreciate the now three unappreciated findings from the PLCO (Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial) PSA screening study. Dietary fiber (especially from cereal and fruits) appeared to reduce the risk of colon cancer and physical activity / exercise reduces the risk of having to get up at night to go number one (aka "makes your bladder flatter"…) and now coffee intake appears to reduce the risk of dying younger from all -causes![1] We have a trifecta folks!

Again, do you remember the USPSTF conclusion that PSA screening should not be done based on the results of two major screening studies, one from Europe and one from the US known as the PLCO? Well, the PLCO researchers did an amazing job of also looking at other things that could impact your health. So, again while many people are out there complaining about PSA screening based on the PLCO study we should all take time once again to appreciate the newest of the now three amazing findings from this same study, and that is that COFFEE (about two or three cups a day caffeinated or decaffeinated) could be associated with a lower cause of death from all causes! And, the researchers also appeared to find a reduction in the risk of death from heart disease, chronic respiratory diseases, diabetes, pneumonia and influenza, and intentional self-harm. The authors concluded by stating that coffee intake could reduce the risk of dying by reducing inflammation, improving lung function, insulin sensitivity and reducing depression. Wow! And Wow spelled backwards!

So, now this same PSA screening study found that if you exercise, you can urinate like a younger version of you, and if you eat more dietary fiber it could reduce your risk of colon cancer and now by drinking coffee in moderation, it could make you live longer? I need to go before I am latte (get it?) for work but the next time you see me, I will have a coffee in one hand and All-Bran buds cereal in the other while walking on a treadmill! Viva Coffee! Viva Coffee! Viva Coffee! It is always more impactful to repeat something three times… three times…three times!

Reference

1. Loftfield E, Freedman ND, Graubard BI, et al. Association of coffee consumption with overall and cause -specific mortality in a large US prospective cohort study. Am J Epidemiol 27 November 2015; Epub.

Common Therapy for Prostate Cancer May Raise Risk of Alzheimer's

This was the conclusion of a new Journal of Clinical Oncology study led by the University of Pennsylvania (UPenn) that analyzed the medical records of two large US hospital systems. The study also found the longer the men were on ADT, the more likely they were to be diagnosed with Alzheimer's disease in the years that followed.

Researchers say their investigation – the first to look at a link between ADT and Alzheimer's disease – is consistent with other evidence that low levels of testosterone may weaken resistance to the neurodegenerative disease in the older brain.

They say while their findings do not prove ADT causes Alzheimer's, they clearly point to the possibility and

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Decline in Prostate Cancer Screenings & Diagnoses *(Continued from page 1)*

get screened," he added. "I think it's terrible to tell a man he can't get screened."

The study found that 30.8% of men ages 50 or older reported getting the PSA test in 2013, down from 37.8% in 2010 and 40.6% in 2008. It also found that the rate of prostate cancer diagnoses in that age group fell from 534.9 per 100,000 men in 2005 to 416.2 in 2012. About 33,519 fewer men received a diagnosis of prostate cancer in 2012 than in 2011, the researchers estimated. A second study in the same journal found a similar drop in the proportion of men who had the PSA screening.

Many studies have shown that if PSA screening saves lives, the number is very small, Brawley said. At the same time, radical prostatectomy (RP) and radiotherapy (RT) for the disease often lead to side effects that affect quality of life. Up to 50% of men who are treated by RP or RT may experience impotence or urinary incontinence. Some have bowel problems.

"Screening is really good at finding cancer that doesn't need to be cured," Brawley said. "But for some men, hearing a diagnosis of cancer and doing nothing but monitoring it is too difficult for them to handle."

Major medical organizations remain split on guidelines, with some cancer and urology groups recommending a less absolute position on routine screening. Matt Tollefson, an associate professor of urology at the Mayo Clinic in Minnesota, said that he recommends "selective" PSA testing for men at high risk for the disease, including African Americans and men with a family history of the disease.

Tollefson said that in past years, the pendulum clearly had swung too far toward routine screenings, which resulted in overtreatment. "Now the question is how far back it should go," he said. "Time will tell what happens to prostate cancer mortality, as well as illness," he said.

In an editorial accompanying the studies, David F. Penson of Vanderbilt University's department of urologic surgery said "there is reason to be concerned" about both the drop in screenings and the decline in cancer diagnoses.

"It is time to accept that prostate cancer screening is not an all or none proposition and to accelerate development of personalized screening strategies that are tailored to a man's individual risk and preferences," Penson said in the editorial.

The Washington Post
7 November 2015

AS & Low-Risk Prostate Cancer *(Continued from page 1)*

AS has been very different from that reported in the current study. "When we started the program 20 years ago, there was a tremendous amount of criticism of AS so we wanted to make absolutely sure that these patients were followed carefully and we have full-time program coordinators and a number of other individuals who help ensure patients comply with the program," said Carter.

Results at JHU, published earlier this year, showed that just two out of 1,298 men enrolled in the AS program had died of prostate cancer and only three developed metastatic disease. "So we're very comfortable with this treatment option and we have demonstrated the safety of the program," Carter said. Still, he added, "I think the study does suggest that there is less than ideal high quality monitoring of a substantial proportion of men who undertake AS."

Researchers identified 45,408 men from Surveillance, Epidemiology, and End Results (SEER) Medicare data who were diagnosed with prostate cancer between 2004 and 2007 with follow-up of Medicare services through 2009. Most of the cohort were between the ages of 70 and 74 years and had T1 tumors and Gleason grade ≤6 disease. Less than 10% of the overall cohort was treated with WW/AS. In men assigned to WW/AS, the mean number of PSA tests done was 2.6 and the mean number of office visits was 2.6 within two years of their diagnosis. However, only 13% of the men in this cohort had a second biopsy within two years of their diagnosis.

Of men on WW/AS having Gleason scores 6, 7, and 8 to 10, from 66% to 71% did not receive at least four PSA tests and 39% to 46% did not attend four or more visits within two years of diagnosis. In contrast, there was a significant increase in surveillance intensity in treated patients according to Gleason score.

Not surprisingly, the intensity of the surveillance given was mediated by proxies of life expectancy including age and comorbidity. For example, men who were 80 years of age and older were 65% less likely to undergo AS than younger men;. Similarly, men with a Charlson score of 1 were 41% less likely to undergo AS. Interesting, nearly one-third of men originally assigned to WW/AS dropped out of AS and were treated aggressively.

Chamie cautioned that two-year follow-up in study participants ended six years ago and thus may not be representative of what is happening today. Other limitations to the study include the fact that the SEER-Medicare database is limited to men ages 65 and older and results may not be generalizable to younger men who are diagnosed with prostate cancer.

Furthermore, neither SEER nor Medicare explicitly identifies those men who are undergoing WW/AS; rather investigators imputed this treatment category back on the lack of any treatment over a two-year period after diagnosis. In point of fact, it is entirely possible that at least some of these men either refused or were not offered treatment, were lost to follow-up, or were treated but had their care paid for by another insurer.

The analysis was also done on a Medicare fee-for-service population and findings may not apply to patients treated under other models.

MedPage Today
4 December 2015

New Screening Model *(Continued from page 1)*

plasma protein biomarkers (PSA, free PSA, intact PSA, human kallikrein 2, beta-microseminoprotein, and macrophage inhibitory cytokine 1), as well as for 232 single-nucleotide polymorphisms, and analyzing clinical variables (age, family history, previous prostate biopsy and prostate examination results).

"STHLM3 was done in two separate phases," Dr. Grönberg and colleagues report. The first phase involved a training cohort consisting of 11,130 men recruited to the STHLM3 study in 2012–2013; the second phase involved 47,688 men who made up the validation cohort, which was used to prospectively test the STHLM3 algorithm.

On the basis of PSA test results, the STHLM3 model, or both, 7,606 of the 47,688 (16%) men in the validation cohort were referred for urologic consultation for further evaluation. Prostate biopsy samples were taken in 71% of this group. In a multiple logistic regression model, "all variables used in the STHLM3 model were significantly associated with high-risk prostate cancers ($P < 0.05$)," the authors note. "The STHLM3 model did significantly better than PSA testing in detecting high-risk prostate cancers ($P < 0.0001$)," they add.

Dr. Grönberg and colleagues also found that the STHLM3 model would reduce the number of biopsies and benign biopsy results by 32% and 44%, respectively in comparison with standard PSA screening. "Of the 603 high-risk cancers identified by the STHLM3 model, 124 (21%) were identified in the PSA range 1-3 ng/mL," they indicate. Use of the STHLM3 model could also result in a 17% reduction in the number of Gleason score 6 prostate cancers, for which biopsy would normally be performed following PSA testing alone. Of those Gleason score 6 cancers that were not diagnosed by the STHLM3 model, all were less than 10 mm in total length, suggesting that most were clinically insignificant.

As the authors point out, a prostate biopsy can cause pain and rectal bleeding and can increase the risk for infection. "The improved specificity of the STHLM3 model could result in savings in terms of reduced treatment morbidity, costs to the individual patient, and to the health-care system," Dr. Grönberg stated.

Commenting on the study in an accompanying editorial, Alastair Lamb, MBChB, PhD, University of Cambridge and CRUK Cambridge Institute, United Kingdom, and Ola Bratt, MD, Lund University, Sweden, point out that the STHLM3 study adds evidence supporting strategies to reduce the negative effects of prostate cancer screening. On the other hand, Dr. Lamb did not feel that the STHLM3 provides the final answer to the problems inherent in screening for prostate cancer at a population level.

One of the shortcomings of the current STHLM3 model is that calibration of the algorithm still led to the detection of many Gleason score 6 cancers – indeed, more than half of the cancers detected using the STHLM3 model were Gleason score 6 tumors. "Given that we are increasingly confident that men with Gleason 6 tumors don't need any treatment at all, we need to ask, do they need to have their cancers detected in the first place," Dr. Lamb said. Similarly, many of the cancers detected using the STHLM3 model

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Doctor Chodak's Bottom Line *(Reference Key: page number and first few words of article title)*

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

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

P1 "Active Surveillance…" As active surveillance gains acceptance throughout the world for a large percentage of men with low-risk disease, it is valuable to assess who is doing it, how often it is being used and how well it is being done. The article by Chamie suggests that there is considerable need for improvement, at least as judged by SEER data from 2004-2007.

Researchers found that less than 10% of seemingly eligible candidates were managed with AS and of those doing so, follow-up studies were underutilized according to current guidelines. The authors were careful to point out that AS was still evolving during the study period so it might not represent what is done in current practice. In addition, the population was older, so again the results may not be generalizable to the entire population of prostate cancer patients. It should be acknowledged that AS is still evolving. Many questions remain unanswered, including what is the best way to provide follow-up. Hopefully, those answers will be forthcoming.

The Bottom Line: If a man is considering AS, a careful discussion is needed between the doctor and the patient so he becomes aware of the current method for proper follow-up testing.

P1 "After USPSTF…" Following the USPTF change in screening recommendations, the use of PSA screening and the diagnosis of prostate cancer appears to have declined. Many people have been upset by those recommendations and are troubled by the forthcoming consequences. However, the article by Brawley and co-workers raises an important point. The observed decline in screening is a good thing if the decision not to screen occurs after a balanced discussion of the pros and cons with the treating physician. Whether or not that is happening is unclear, but the pessimist in me doubts it is occurring as often as needed. It is definitely time consuming and primary care doctors may not perceive it is the best use of their time.

Thinking has clearly changed now compared to 10 or 15 years ago when any questions about the value of screening were heavily criticized. Now the latest data are likely to result in even more vocal concerns by supporters of PSA screening.

The concept of individualized screening is growing. Many doctors suggest that high-risk men should still be screened aggressively, and older, less healthy men should not. My concern about that approach is that it lacks any supportive data to showing that the benefit outweighs the harm in those men. Just because African-American men or those with a family history are more likely to be diagnosed with prostate cancer, does not mean they are more likely to benefit from screening. Without supporting data, we may repeat an earlier error when PSA was discovered and recommending generalized screening without proof it was the right thing to do. Let's hope that is not the case.

The Bottom Line: Doctors are following USPTF recommendation against routine screening and it is unknown if men are properly counseled and if mortality rate will rise significantly.

P1 "New Model…" A new model from Sweden for prostate cancer screening called STHLM3 is showing promise because of improved accuracy compared to the traditional PSA. Using this approach, the detection of Gleason 3+3 was lowered and the biopsy rate was reduced, both being known problems with traditional screening. Is it ready for prime time as a replacement for PSA? The answer is unknown, as many questions still need to be answered. The authors did find more high-risk cancers in men with a PSA of only 1-3 ng/mL, which would have been missed if a PSA cutoff of 4 ng/mL were used. The most critical questions are whether using this approach would save more lives and how many men will still be diagnosed that would not need treatment. Answering them will require a lengthy randomized study. Otherwise we will never know.

The Bottom Line: More information is needed to assess the overall value of the STHLM3 screening test.

P2 "Biochemical; Genomic…" Although surgery cures the majority of men, some do recur and progress. Knowing who is likely to recur before it occurs provides an opportunity to intervene and possibly alter the outcome, or conduct clinical studies to identify treatments likely to work. Aguilera et al found the strongest predictors of recurrence were positive margins and Gleason score. Glass et al used a new method called Decipher either alone or in combination with the CAPRA score to discriminate between men at low and high risk of recurrence. However, there are numerous problems with these studies. Starting with Decipher, a 2.6% recurrence rate occurred in men with a low-risk result compared to 13.6% for the high-risk result. That means doing the test and possibly treating only men with a high-risk result would still mean that five out of every six men treated based on the test would not be getting a recurrence and the treatment would be unnecessary. Similar problems occur with using the data from the Aguilera study. What does this mean? These data are best used to design a prospective study in which only the high-risk group is randomized but without such a study, these types of studies do not really help with patient management.

The Bottom Line: Tests that help identify risk of recurrence after local therapies are important but much more is needed to know if the tests are truly helpful.

Alzheimer's Disease

(Continued from page 3)

call for more research to investigate the link further. Lead author Dr. Kevin T. Nead, a radiation oncologist in UPenn's Perelman School of Medicine, says their aim is to contribute to a discussion about the risks and benefits of ADT, and "Based on the results of our study, an increased risk of Alzheimer's disease is a potential adverse effect of ADT, but further research is needed before considering changes to clinical practice."

At any given time, there are around half a million men in the US taking ADT, a com-

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Non-Steroidal Antiandrogen vs. LHRH-A	Apr
Normal Erection after Radical Prostatectomy is Rare	Jun
Obesity Increases the Risk of High-Grade Prostate Cancer	Jan
Occult T3 Vs Clinical T3 Tumors & Postprostatectomy Survival	Aug
Patient Scar Satisfaction According to Type of RP	Feb
PDE5-I and Melanoma Risk	Aug
PDE5-I Use & Risk of BCR Following Radical Prostatectomy	Mar

Name of Article	Month
Persistent Positive Biopsies after High-Dose Rate Brachytherapy	Apr
Photodynamic Diagnosis of Shed Prostate Cancer Cells in Urine	Jan
POM Loses Bid to Claim Health Benefits	Mar
Positive Surgical Margins Postprostatectomy & Mortality	Mar
Predicting Unfavorable Prostate Cancer Before AS	Aug
Prostate Biopsies May Be More Accurate at Academic Centers	Mar
Prostate Cancer Genetically Divided into Five Distinct Subtypes	Sep
Prostate Cancer Testing Falls after USPSTF Recommendation	Sep
Prostate Cancer Treatment with New Injectable Gel	Jun
Prostate Tumors with Genetic Abnormalities & Olaparib	July
Prostatectomy Impairs Sex for Both Partners	Apr
PSMA Expression is Homogeneous in Primary Prostate Cancer	Oct
Radiographic Progression-Free Survival & Abiraterone Response	Apr
Radiotherapy after Prostatectomy: Debate Over Timing	May
Randomized Phase II Trial of Lycopene Extract in High-Grade PIN	Nov
Rate of Observation for Prostate Cancer Increasing	Apr
Sexual Partners, Transmitted Infections & Prostate Cancer Risk	Jan
Silicon and Bone Health	Nov
Some Low-Risk Prostate Cancers Require Closer Scrutiny	Sep
Statins May Slow Prostate Cancer Progression Following ADT	July
Study of Prostate Cancer in Medically Underserved Men	Aug
Study Raises Questions about ADT in Certain Prostate Cancers	Nov
Surveillance May Be Safest Option for Low-Risk Prostate Cancer	Feb
T Levels Improve in Obese Men after Bariatric Surgery	Nov
Timing of Androgen Deprivation ("TOAD") Phase III Trial	July
Tissue Choline Kinase-A & Prognosis of Prostate Cancer	Nov
Two Prostate Cancer Tests 'Not Clinically Useful' Says NICE	Feb
Two Years of ATT Improves Survival in Post-surgical Recurrence	Dec
Updated Results form the Spanish Branch of the ERSPC Trial	Jun
Urine Assay Promising As Test for High-Grade Prostate Cancer	July
Weak Evidence Favors Intermittent ADT for Advanced PCa	Nov

New Screening Model

(Continued from page 4)

were Gleason score 7 (3 + 4). "And it's become increasingly apparent that Gleason 7 (3 + 4) cancers behave more like Gleason 6 tumors as well," Dr. Lamb noted.

By recalibrating the algorithm, Dr. Lamb felt that the diagnosis of Gleason 6 tumors and even the less virulent forms of Gleason 7 tumors could be attenuated, which would be a desirable endpoint. But he would also like to see a modified or refined algorithm used in a study in which the primary endpoint was survival, rather than a pathologic endpoint.

"Next-generation prostate cancer screening involves risk stratification, risk differentiated screening algorithms, and sequential testing to select men for biopsy," Dr. Lamb and Dr. Bratt conclude.

Medscape Medical News
23 November 2015

ADT May Raise Risk of Alzheimer's Disease

(Continued from page 5)

mon treatment for prostate tumors. The therapy suppresses production of androgens, male hormones that normally help stimulate the growth of prostate cells, including cancerous ones.

However, major reduction of male hormone levels can also lead to adverse side effects. There is evidence that low levels of androgens (primarily testosterone) are linked to obesity, diabetes, depression, impotence, heart disease and high blood pressure.

More recent studies have also linked low testosterone to problems with thinking and memory. There is also evidence that men who develop Alzheimer's disease tend to have lower levels of testosterone, compared with counterparts who do not develop the disease.

The new study analyzes data from two large sets of medical records: one covering 1.8 million men from the Stanford health system and the other covering 3.7 million men from Mt. Sinai Hospital in New York City. From this large pool of over five million patient records, researchers found around 18,000 prostate cancer patients, including 16,888 whose cancer had not begun to spread. Within this pool, they also found 2,397 patients who had been treated with ADT.

Such a large data set allowed the researchers to compare the ADT patients with a matched control group of patients who did not have ADT but were similar in age and other factors. Their analysis showed that compared to counterparts who did not have the therapy, the men who underwent ADT were significantly more likely to be diagnosed with Alzheimer's disease in the years following the start of their hormone-lowering therapy.

The researchers found the men on ADT were about 88% more likely to be diagnosed with Alzheimer's disease than men who were not on ADT. They also found a dose-response effect in that the longer the ADT lasted, the higher the likelihood of being diagnosed with Alzheimer's, to the point where the patients who were on ADT the longest had double the risk of Alzheimer's than those who did not have ADT.

"It's hard to determine the precise amount of increased risk in just one study and important to note that this study does not prove causation," commented Dr. Nead. "But considering the already-high prevalence of Alzheimer's disease in older men, any increased risk would have significant public health implications."

Medical News Today
8 December 2015

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