US TOO® PROSTATE CANCER EDUCATION & SUPPORT

HOTSHEET

MARCH 2013

FUNCTIONAL ISSUES SIMILAR WITH SURGERY AND RADIATION FOR PROSTATE CANCER

Men with localized prostate cancer have declines in sexual, urinary, and bowel function over time, whether they choose radical prostatectomy (RP) or radiation therapy (RT), data from a large cohort study showed.

RP increased the odds of urinary incontinence (UI) and erectile dysfunction (ED) at 2 and 5 years compared with RT, which was associated with an increased likelihood of bowel dysfunction at 2 and 5 years. However, the extent of functional decline did not differ significantly at 15 years, regardless of the initial radical therapy, as reported online in the New England Journal of Medicine (DOI: 10.1056/NEJMoa1209978).

"Since the median life expectancy after treatment for prostate cancer is 13.8 years, a careful evaluation of long-term functional outcomes is critical to an understanding of the comprehensive experience of men living with a diagnosis of prostate cancer," David F. Penson, MD, of Vanderbilt University in Nashville, TN and colleagues noted in their introduction.

To inform on long-term outcomes after treatment for localized prostate cancer, Penson and colleagues analyzed data from the Prostate Cancer Outcomes Study (PCOS), a population-based cohort study involving men 55 to 74 years

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'SMARTER' PSA TESTING STRATEGIES PROPOSED

In the quest to identify men at the greatest risk for prostate cancer, more aggressive approaches may not be the answer. Instead, some "smarter" strategies proposed in a new study could reduce potential harms associated with PSA testing without diminishing the estimated percentage of lives saved.

There is little consensus on the optimal approach to PSA testing, and the US Preventive Services Task Force recently stated that the current protocol produces more harm than good. Therefore, Roman Gulati, MS, from the Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA, and colleagues designed a mathematical model to determine the best combination of testing parameters. They reported their findings online February 4 in the *Annals of Internal Medicine*.

"Few data exist to help clinicians have nuanced conversations with patients about whether and how to have prostate cancer screening," the authors write. "Data from this study may inform conversations clinicians have with men about whether and how they should be screened," they continue.

The team used microsimulation modeling to identify potentially smarter screening strategies. They assessed 32 different permutations of PSA testing variables: age to start screening (e.g., 40

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FOLLOW-UP TO REDUCE STUDY SHOWS LOW RATE OF PROSTATE CANCER DIAGNOSIS

The four-year REDUCE (REduction by DUtasteride of prostate Cancer Events) clinical study evaluated prostate cancer risk reduction in men taking dutasteride, a 5-alpha-reductase inhibitor (5ARI) typically used to treat enlarged prostate. REDUCE results showed that dutasteride decreased the risk of biopsy detectable prostate cancer by 22.8 percent compared to a placebo group, but concerns remained about the drug's effectiveness. Results from a follow-up study were published in *The Journal of Urology* (Vol.189, pp. 871-878, 2013).

"The REDUCE Follow-up Study was a two-year observational follow-up of men who participated in the four-year REDUCE trial," says lead investigator Robert L. Grubb III, Associate Professor of Surgery (Urology), Washington University of Medicine in St. Louis, MO. "The primary objective was to collect data on the occurrence of new cases of prostate cancer for two years beyond REDUCE."

Nearly 2,800 men from the REDUCE study participated, representing extension safety and at-risk populations. In the original study, about half were treated with dutasteride and the remainder received a placebo.

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POPULATION-BASED 10-YEAR ONCOLOGIC OUTCOMES AFTER LOW-DOSE-RATE BRACHYTHERAPY FOR LOW-RISK AND INTERMEDIATE-RISK PROSTATE CANCER

Morris WJ, Keyes M, Spadinger I, et al

Cancer 26 December 2012; Epub ahead of print

Background: The objective of this study was to report the rates of disease-free survival (DFS), cause-specific survival (CSS), and overall survival (OS) after low-dose-rate (LDR) prostate brachytherapy (PB).

Methods: Data from 1006 consecutive men with prostate cancer who received LDR-PB and underwent implantation on or before October 23, 2003 were extracted from a prospective database on November 11, 2011. The selected men had low-risk (58%) or intermediate-risk (42%) disease according to National Comprehensive Cancer Network (NCCN) criteria. Phoenix threshold was used to define biochemical relapse. Sixty-five percent of men received 3 months of neoadjuvant androgen-deprivation therapy (ADT) and 3 months of concomitant ADT. Univariate and multivariate analyses are reported in relation to patient, tumor, and treatment variables.

Results: The median follow-up was 7.5 years. By using Fine and Gray competing risks analysis, the 5-year and 10-year actuarial DFS rates were 96.7% (95% confidence interval [CI], 95.2%-97.7%) and 94.1% (95% confidence interval, 92%-95.6%), respectively. When applied to the whole cohort, none of the usual prognostic variables, including dose metrics, were correlated with DFS. However, in both univariate and multivariate models, increasing dose was the only covariate that correlated with improved DFS for the subset of men (N = 348) who did not receive ADT (P = .043). The actuarial 10-year CSS rate was 99.1% (95% CI, 97.3%-99.7%). The overall survival rate was 93.8% at 5 years (95% CI, 92%-95.1%) and 83.5% at 10 years (95% CI, 79.8%-86.6%). Only age at implantation (P = .0001) was correlated with OS in multivariate analysis.

Conclusions: In a consecutive cohort of 1006 men with NCCN low-risk and intermediate-risk prostate cancer, the actuarial rate of recurrent disease after LDR-PB was approximately 3% at 5 years and 6% at 10 years.

LOW NEUTROPHIL COUNT PREDICTS A POSITIVE PROSTATE BIOPSY

Fujita K, Imamura R, Tanigawa G, et al

Prostate Cancer Prostatic Dis 15: 386-90, 2012

Background: Asymptomatic prostatic inflammation may cause increased PSA in some men, leading to unnecessary prostate biopsy. We investigated whether the differential white cell count could predict the result of prostate biopsy.

Methods: Prostate needle biopsy was carried out in 323 Japanese men with elevated PSA levels or abnormal digital rectal findings. White blood cell count (WBC), differential white cell count (neutrophils, lymphocytes, basophils, eosinophils, and monocytes), and serum C-reactive protein level were assessed for associations with biopsy findings.

Results: In all, 203 (62.1%) were positive for prostate cancer. WBC, neutrophil count (NC), age, PSA, prostate volume, and PSA density (PSAD) were associated with the results of biopsy (P<0.05). Multivariate analysis showed that NC, age, PSA, prostate volume and PSAD were independent predictors. When the cut-off NC was set at 2900/μl, 78 of 104 men (75.0%) with a NC below this value had a positive biopsy, while 125 of 219 (57.0%) men with a NC above this value were positive. The area under the receiver-operator characteristics curve (AUC) for the predicted probability of a positive biopsy for prostate cancer according to the optimum logistic model was 0.83 (95% CI 0.78–0.87), while the AUC for PSA was 0.70 (95% CI 0.64–0.76) and for PSAD was 0.79 (95% CI 0.74–0.84).

Conclusions: An elevated NC may be a good indicator of a benign prostate biopsy. Men with a low NC and an increase of serum PSA should strongly be considered for biopsy.

FUNCTIONAL OUTCOMES

(Continued from page 1)

of age diagnosed with prostate cancer in the 1990s and followed prospectively for 15 years. The final analysis involved 1,164 men who had undergone RP and 491 who opted for RT and were treated within 12 months of diagnosis.

At baseline assessment, all PCOS participants provided information about prediagnostic urinary, sexual, and bowel function. Men were contacted at 1, 2, 5, and 15 years after diagnosis and asked to complete surveys related to disease-specific health-related quality of life.

At 15 years, 322 men (27.7%) in the RP group had died, as had 247 (50.3%) who underwent RT. Overall survey response rates were 87.5% at 2 years, 83.3% at 5 years, and 60.3% at 15 years. At the 2-year mark, the RP group was more than 6 times as likely to have UI as the RT group (OR 6.22, 95% CI 1.92 to 20.29). At 5 years, the odds for UI remained 5 times higher in the RP group (OR 5.10, 95% CI 2.29 to 11.36).

The odds for ED also were significantly increased after RP compared with RT at 2 and 5 years but was associated with significantly lower odds of bowel urgency at 2 year and 5 years compared with RT. At the 15-year follow-up, all of the significant differences had disappeared, although absolute numbers continued to suggest between-group differences:

- Urinary incontinence – 18.3% with RP vs. 9.4% with RT (OR 2.3, 95% CI 0.9 to 6.2)
- Erectile dysfunction – 87.0% vs. 93.9% (OR 0.4, 95% CI 0.1 to 1.2)
- Bowel urgency – 21.9% vs. 35.8% (OR 0.98, 95% CI 0.5 to 2.1)

Advancing age almost certainly contributed to the high rates of functional problems at 15 years, Penson acknowledged. However, case-control studies by PCOS investigators showed that prostate cancer patients had worse functional outcomes at 5 years vs. age-matched men who had not had prostate cancer.

"While there's definitely an aging effect, I think that we still have to say that some of this is also directly related to primary treatment, secondary treatment, or prostate cancer itself," said Penson.

MedPage Today, 30 January 2013

REGAINING CONTINENCE FOLLOWING PROSTATE SURGERY

Jeff Pepper, President, Three Ten LLC

As all prostate surgery survivors know, urinary incontinence (UI) is probably the most unpleasant long term consequence of the surgery, often lasting months or years. Despite improvements in surgical techniques, UI remains a serious impairment to quality of life for those of us who have undergone a radical prostatectomy (RP).

Nearly all men have some degree of UI after RP, because the surgery removes two of our three mechanisms for controlling urine flow. First, the internal urinary sphincter (IUS), an involuntary muscle which exists in men but not in women, is removed or damaged so it can no longer stop urine flow. Second, the lobes of the healthy prostate exert mild pressure on the urethra, also somewhat impeding urine flow. When the prostate is removed, the pressure that it causes is removed. This can be a relief for men who were suffering from impaired urine flow due to an enlarged prostate and find that the urine flow is now unimpeded. However, it's a mixed blessing, because, well, the flow is unimpeded.

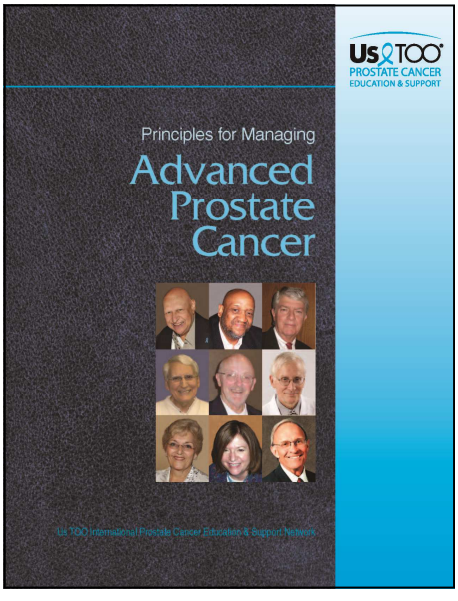
So after RP, the only remaining barrier to urine flow is the external urinary sphincter (EUS), a voluntary muscle. Every man is somewhat familiar with this muscle, as it's the one that we use to consciously halt urine flow. (Incidentally, because women don't have an UIS or a prostate, the EUS is their only method for stopping urine flow, and they learn from early childhood how to use it.)

Some men are not used to using this muscle on a constant basis, as they have relied exclusively on the IUS for their entire lives. It's easy to tell if you are one of these men. Just cough, and see whether you involuntarily contract your EUS. Most men do, but some don't. For those who don't, the EUS muscle is relatively weak and needs to be strengthened through exercise. But more importantly, these men never established a mental habit of keeping the EUS contracted. And it can be a real challenge to retrain yourself at age 50, 60 or 70 to keep a muscle contracted that you've been barely aware of for most of your life.

So the challenge for prostate surgery survivors is to learn where the EUS is, strengthen the muscle, and establish a mental habit of keeping the muscle contracted all day – when walking, when running, when lifting, and so on. For at least 10% of men who have prostate surgery, this process takes more than a year. Progress is gradual, often so gradual that men cannot tell from week to week or month to month if they are getting better.

To help men (and women) get a clearer idea of their progress in overcoming UI, we developed iDry. iDry is a free software app that runs on the Apple iPhone, iPad and iPod Touch. It provides an easy way to log every time you change a pad and diaper, and how wet it was. The app then calculates your total urine lost per day, charts your progress over time, and predicts when, if trends continue, you will be completely dry. The app also can track the effectiveness of different interventions, including diet (such as restricting caffeine and alcohol), physical exercises (such as Kegels), drugs, surgeries, and alternative therapies. You can email results to yourself or your doctor, and you can set the app to give you regular reminders to do your pelvic floor exercises.

iDry was developed by Three Ten LLC with assistance from Dr. Joel Nelson, Chair of the Department of Urology at the University of Pittsburgh Medical Center, and was funded by a grant from the National Institute on Aging. To learn more, visit www.idry.org, or search for "iDry" in the Apple App Store.



STUDY SHOWS ID ERRORS IN PROSTATE BIOPSIES

As many as 3.5% of prostate biopsy specimens were contaminated or inadvertently switched with that of another patient, according to a review of 13,000 samples from 54 laboratories.

The overall error rate was less than 1%, but rates among different types of labs ranged as high as 3.51%. No laboratory included in the study had an error-free performance record.

Institutional approval for the study required investigators to remove all identifying information from the specimens. Consequently, the impact of the laboratory errors could not be assessed, as reported online in the *American Journal of Clinical Pathology*.

"It is possible that in a subset of cases, the adenocarcinoma from the foreign patient that was the source of the extraneous tissue exhibited sufficiently similar characteristics of the target patient such that either patient's diagnosis would have resulted in the same course of therapy," John D. Pfeifer, MD, PhD, and Jingxia Liu, PhD, of Washington University in St. Louis, MO wrote of their findings.

"Regardless of the portion of cases in which patients may have, by chance, received the correct treatment despite the specimen identity error, the fact remains that ... a diagnosis was assigned to the wrong patient with no knowledge or even suspicion of the error that had occurred."

The study examined the frequency of occult "specimen provenance complications" (SPCs), errors that occur without any indication of a problem. SPCs arise when specimens are matched to the wrong patients (type 1 error) or when one patient's specimen is contaminated by tissue from one or more other patients (type 2 error).

SPCs have obvious implications for patient safety and medicolegal actions, the authors noted in their introduction. However, the frequency with which these errors occur has remained unclear.

To describe the rates of both types of SPCs, Pfeifer and Liu analyzed data for 13,000 prostate biopsy specimens obtained in routine clinical practice. The

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PATHOLOGICAL AND BIOCHEMICAL OUTCOMES AFTER RADICAL PROSTATECTOMY IN MEN WITH LOW-RISK PROSTATE CANCER MEETING THE PROSTATE CANCER INTERNATIONAL ACTIVE SURVEILLANCE CRITERIA

Mitsuzuka K, Narita S, Koie T, et al

BJU Int 15 January 2013; Epub ahead of print

What's known on the subject? And what does the study add?: Active surveillance (AS) has been widely accepted as a treatment tool for low-risk prostate cancer, and use of the Prostate Cancer Research International: Active Surveillance (PRIAS) criteria can select smaller and less aggressive tumours in low-risk disease. The study shows the pathological outcomes of radical prostatectomy (RP) for men with low-risk disease who met the PRIAS criteria. It found that ~20% had unfavourable pathological features and only 30% satisfied insignificant cancer criteria with pT2 stage, a Gleason score ≤6 and tumour volume <2.5 mL. It concludes that close follow-up including repeat biopsy or MRI is necessary to minimize unexpected progression of disease.

Objective: To assess the effectiveness of the PRIAS criteria in identifying indolent cancer.

Patients and Methods: Data from 1268 men undergoing RP without neoadjuvant therapy were retrospectively reviewed. Within this cohort, men with low-risk disease (N=211) were classified according to whether they met (Group A, N=87) or did not meet (Group B, N=124) the PRIAS criteria. Pathological upstaging, upgrading, tumour volume and 5-year PSA recurrence-free survival (RFS) were compared between the 2 groups, and factors that predicted upstaging, upgrading and PSA recurrence were analysed by univariate and multivariate methods.

Results: Pathological T3 stage was present in 10.3% of men in Group A and in 18.5% of men in Group B (P=0.08). Gleason score upgrading to 4+3 or greater was seen in 19.5% of Group A and in 29.9% of Group B (P=0.01). The mean (range) tumour volume was 0.81 (0.03-5.09) mL in Group A and 1.40 (0.04-8.21) mL in Group B (P <0.01). The rates of insignificant cancer with total tumour volume <2.5 mL, Gleason score ≤6 and stage pT2 were 30.6% in Group A and 15.4% in Group B (P=0.07). With a median follow-up of 44 months, the 5-year PSA RFS rates were 91.2% in Group A and 86.4% in Group B (P=0.47). In multivariate analysis, PSA density and the PRIAS criteria were independent factors that predicted upstaging.

Conclusions: Although use of the PRIAS criteria could select more favourable tumours even in low-risk prostate cancer, about one in 5 men had unfavourable pathological outcomes and only 3 in 10 had insignificant cancer. Close and careful follow-up is necessary to avoid misclassification or progression of disease, especially during the first few years of AS.

DOES SUSPICION OF PROSTATE CANCER ON INTEGRATED T2 AND DIFFUSION-WEIGHTED MRI PREDICT MORE ADVERSE PATHOLOGY ON RADICAL PROSTATECTOMY?

Borofsky MS, Rosenkrantz AB, Abraham N, et al

J Urol 26 December 2012; Epub

Objective: To determine whether suspicion for tumor on prostate magnetic resonance imaging (MRI) incorporating T2-weighted imaging (T2-WI) and diffusion-weighted imaging (DWI) predicts more adverse pathology on radical prostatectomy (RP).

Methods: From 2007 to 2009, 154 men underwent 1.5 Tesla pelvic-phased-array MRI of the prostate that included T2-WI and DWI before RP. MRI results were retrospectively reviewed and grouped by degree of suspicion for tumor: no suspicion for tumor (NST, N=15), equivocal suspicion for tumor (EST, N=60), or strong suspicion for tumor (SST, N=79). The NST/EST groups were combined and compared to the SST group. Preoperative variables were used to assemble a multivariate model. Outcomes reflective of adverse pathology included primary Gleason grade (GG) ≥4, pathologic stage ≥pT3, and tumor upgrading.

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PROSTATE CANCER PROGRESSION MAY BE PREVENTED BY A HIGH FIBER DIET

A high-fiber diet may have the clinical potential to control the progression of prostate cancer in patients diagnosed in early stages of the disease.

The rate of prostate cancer occurrence in Asian cultures is similar to the rate in Western cultures, but in the West, prostate cancer tends to progress, whereas in Asian cultures it does not. Why? A University of Colorado Cancer Center study published in the January 2013 issue of the journal *Cancer Prevention Research* shows that the answer may be a high-fiber diet.

The study compared mice fed with inositol hexaphosphate (IP6), a major component of high-fiber diets, to control mice that were not. Then the study used MRI to monitor the progression of prostate cancer in these models.

"The study's results were really rather profound. We saw dramatically reduced tumor volumes, primarily due to the anti-angiogenic effects of IP6," says Komal Raina, PhD, research instructor at the Skaggs School of Pharmacy and Pharmaceutical Sciences, working in the lab of CU Cancer Center investigator and School of Pharmacy faculty member, Rajesh Agarwal, PhD.

Basically, feeding with the active ingredient of a high-fiber diet kept prostate tumors from making the new blood vessels they needed to supply themselves with energy. Without this energy, prostate cancer couldn't grow. Likewise, treatment with IP6 slowed the rate at which prostate cancers metabolized glucose.

Possible mechanisms for the effect of IP6 against metabolism include a reduction in a protein called GLUT-4, which is instrumental in transporting glucose.

"Researchers have long been looking for genetic variations between Asian and Western peoples that could explain the difference in prostate cancer progression rates, but now it seems as if the difference may not be genetic but dietary. Asian cultures get IP6 whereas Western cultures generally do not," Raina says.

Medical News Today, 11 January 2013

REDUCE STUDY FOLLOW-UP

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Shortly after the REDUCE study's conclusion, Dr. Grubb and co-investigators followed participants with a clinic visit. They also conducted up to two annual telephone calls, collecting patient data on prostate cancer events, chronic medication use, prostate specific antigen levels, and serious adverse events. No drugs were administered and no additional biopsies were performed except those "for-cause" when clinically indicated.

Results showed that few new prostate cancers were detected during the two-year follow-up in either treatment group and no deaths were reported. However, the former dutasteride group produced double the number of cancers than the former placebo group (14 vs. 7). Investigators hypothesize that any prostate cancer that may have been suppressed by dutasteride during REDUCE was no longer being suppressed for those subjects who did not continue on 5ARI therapy. To some extent, observations during the follow-up study support this concept.

Using Gleason scores, the system used to evaluate the prognosis of prostate cancer, no high grade prostate cancers (Gleason Score 8-10) were detected. No new safety issues surfaced.

More men from the placebo group underwent biopsy (11.6 percent) than men from the dutasteride group (7.9 percent). A higher incidence of prostate cancer (1.3 percent) was observed in men in the dutasteride group who did not continue 5ARI treatment. Overall, men in either group who took a 5ARI during the follow-up study tended to have fewer cancers.

"Although this study provides real-world observational data for subjects who had been randomized to four years of dutasteride therapy, it has limitations," cautions Dr. Grubb. "Men in the at-risk population had a low risk of prostate cancer diagnosis due to several prior negative biopsies and corresponding conclusions are specific to the population studied. In addition, some men who dropped out of REDUCE early may have been off dutasteride treatment for longer than the two-year observational period."

Medical News Today, 24 January 2013

ASK DOCTOR SNUFFY MYERS

Editors' note: Us TOO has invited certain physicians and others to provide information and commentary for the *HotSheet* to enrich its content to empower the reader. This column contains the opinions and thoughts of its author and is not necessarily those of Us TOO International.

Question 1: What do you think of the Metabolic pH Transfer Factor, Alkaline and Acidic foods diet? Also, why isn't the Navarro Urine Sampling test being used more instead of PSA blood tests?

These options are not commonly used because they are worthless. No one wants to waste their time and money. I have written extensively about the folly of acid and alkaline manipulations. I am frankly tired of repeating this over and over. I will limit my comments to a simple statement: you cannot safely make your body acid or alkaline. I suggest you start by reading the article on "acid-base homeostasis" in Wikipedia. In my opinion, any health care provider that proposes to alter the pH of your body is either incompetent enough not to understand basic biology or a fraud or both.

Question 2: The Robotic process is new, and I have read articles, including the Chodak evaluation, where the issue of infected margins are tough to find with Robotics, and even tougher to find in nodes. The Robotic surgeons have told me that they can find affected areas visually with light and magnification capabilities of the laparoscope. I would like to know your thoughts about this matter.

In skilled hands, robotic prostatectomy is a dramatic improvement over open surgery. The major problem is that this is difficult surgery and too many surgeons are doing this when they lack the skill to do it well. Specifically, I think Dr. Chodak is completely wrong and that the best robotic surgeons are more likely to have clean surgical margins if the capsule has been penetrated.

I see a lot of men with PSA recurrence after surgery. In a vast majority of cases, the recurrent disease is in the lymph nodes in the pelvis or the lower abdomen. I think this proves even the best surgery is ineffective at the detection or treatment of lymph node metastases.

'SMARTER' PSA TESTING

(Continued from page 1)

vs. 50 years), frequency of subsequent testing, age at which to stop testing, and different PSA cutoff values for biopsy referral. They also assessed screening recommendations from the American Cancer Society and the National Comprehensive Cancer Network.

Compared with a reference strategy of annual screening for men aged 50 to 74 years with a PSA cutoff of 4.0 µg/L (4.0 ng/mL) for biopsy, more aggressive strategies decrease prostate cancer mortality. However, the authors write, "the harms of unnecessary biopsies, diagnoses, and treatments may be unacceptable."

Instead, less frequent testing and more conservative considerations for biopsy, particularly in older men, translated into "substantial improvements" in the risk–benefit tradeoff of PSA testing by preserving screening's survival advantage. For example, screening using an age-dependent PSA cutoff after age 69 reduced overdiagnosis risk from 3.3 to 2.3% vs. the reference protocol. At the same time, the risk for prostate cancer death only increased from 2.15 to 2.3%

John Concato, MD, MPH, from the Veterans Affairs Connecticut Healthcare System, West Haven, and Yale University, New Haven, CT, wrote an accompanying editorial. In that he stated, "The model itself is mathematically meticulous and conceptually interesting, and the conclusions are reasonable – but the corresponding clinical relevance is limited. The results, presented as tradeoffs and involving calculations that often differ by only a fraction of a percentage point, are not likely to change clinical practice."

An inability to assess cancer grade progression or clinical stage of disease were among the study's potential limitations.

Medscape Medical News, 4 February 2013

Want to learn more about local prostate cancer support group activities? Read the

CHAPTER NEWS!

at www.ustoo.org!

DOC MOYAD'S WHAT WORKS & WHAT IS WORTHLESS COLUMN, ALSO KNOWN AS "NO BOGUS SCIENCE" COLUMN

"Wait? If I exercise while I am on a statin drug then the risk of dying younger goes down another 70%?! You have to be kidding me Moyad !"

Mark A. Moyad, MD, MPH, Univ. of Michigan Medical Center, Department of Urology

Editors' note: Us TOO has invited certain physicians and others to provide information and commentary for the *HotSheet* to enrich its content to empower the reader. This column contains the opinions and thoughts of its author and is not necessarily those of Us TOO International.

Bottom Line: A new prospective study from the Veterans Affairs Medical Center found a lower risk of dying from any cause when on a statin (cholesterol lowering drug). However, the risk of death further decreased with fitness! In fact, the best fit individuals had a 70% reduction in death compared to the least fit! So, if you are on one of these drugs, get off your gluteus maximus and also give me 30-60 minutes per day! Ahhh I sound like a US Army Drill Sergeant! Good! Now drop and give me 25 pushups or 25 dollars (research and beer funds are low these days)!

Do you know how many prostate cancer support group or medical meetings I have lectured to over the last 25 years? 1000? 2000? 3000? Maybe. Do you know how many men in those groups, be it men with prostate cancer or health care professionals, have come up to me after my lecture and asked me why they need to really exercise if their cholesterol is already so low on a statin? 1000? 2000? 3000? YES! When did we reach the point where we thought a pill was going to do all the work and we did not have to invest in our health? I have always referred to studies that clearly showed that taking a magic pill is never enough and there are subtle but large rewards for those that invest added workout time in their lives. Now, here comes arguably the most powerful study to ever show that exercise matters even when taking a pill. A 70% REDUCTION!!! "ARE YOU KIDDING ME?" (John McEnroe Circa 1980 or Bobby Knight when he was the coach of the Indiana basketball team or my dad when I was 16 years old and told him I wrecked the car). This work would win a noble prize if it were all about a pill! The men that were most fit in this study were able to reach 9 MET peaks on an exercise machine, but men that could do just 7 MET also did almost as well. Think about this the next time you get on a treadmill or elliptical machine.

You get 1 MET for sitting on the couch and 3-5 MET for just moving and 5-7 MET for a light jog and 7-9 MET for more hard core sweat-a-lot exercises. The bottom line is that just exercising 30-60 minutes per day basically allows many individuals to reach this exercise capacity. So, the next time you see me at a meeting and ask me if it matters if you exercise despite having such great numbers on a high-dose statin drug I am going to laugh and smile and just go "Hey buddy (or budette), did you read the March issue of the US TOO HotSheet?!" And, then I am going to ask you to give some money and buy me some beer! Ohhh, and then I am going to say "Go Blue" if you are wearing any T-shirt that is from another Big Ten school or any college that is not Michigan. And, then if you are larger than me I am going to start running fast in the opposite direction because I can do 9 METs and more baby!

Reference:

Kokkinos PF, Faselis C, Myers J, et al. Lancet 381: 394-399, 2013.

IS AN EXTENDED 20-CORE PROSTATE BIOPSY PROTOCOL MORE EFFICIENT THAN THE STANDARD 12-CORE? A RANDOMIZED MULTICENTER TRIAL

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Purpose: The aim of this study was to determine the impact of increasing the number of cores from 12 to 20 at initial prostatic biopsy (PB) in men suspicious of prostate cancer (PCa).

Material and methods: From December 2009 to November 2011, patients in 7 centers scheduled for a first PB, with a PSA < 20 ng/mL and no nodule on digital rectal examination, were invited to participate in this superiority trial. Patients were randomized to a 12-core (PB12 group) or a 20-core (PB20 group) protocol. The primary end point was cancer detection rate (CDR). Secondary end points were cancer characteristics, rate of complications and patient's tolerance assessed by a self-completed booklet before PB and at day 5 and day 15.

Results: A total of 339 patients were randomized. Preoperative variables were similar in both groups. Cancer was detected in 71 patients (42.0%) in PB12 group and in 81 patients (48.8%) in PB20 group: the difference was not significant (p>0.2). Gleason score and cancer length measured on PB cores were not significantly different between groups. Although CDR rate was linked to prostate volume, this was not affected by the number of extracted cores (p> 0.4). Complications number and seriousness were comparable in both arms. No significant difference was noted regarding side-effects and tolerance as self-assessed by the patient at day 5 and day 15 following PB.

Conclusions: Our findings suggest that there is no significant advantage in using a 20-core biopsy protocol vs 12-core protocol during an initial PB.

DOCTOR CHODAK'S BOTTOM LINE

Due to an unfortunate accident that injured his knee, Dr. Chodak was unable to submit his regular column before this issue's printing deadline. We all hope he has an uneventful and speedy recovery and look forward to seeing his column in the April 2013 HotSheet.

WORKOUTS CUT PROSTATE CANCER RISK IN WHITES

Another benefit of exercise – at least for Caucasian men – is that it may cut the risk both of developing prostate cancer and having high-grade disease, researchers reported.

In a prospective study, Caucasian men suspected of prostate cancer and scheduled for biopsy were less likely to have the disease if they were at least moderately active, according to Lionel Bañez, MD, of the Durham Veterans Affairs Medical Center in Durham NC, and colleagues.

If they did have cancer, they were significantly less likely to have high-grade disease if they had been working out regularly, Bañez and colleagues reported online in the journal *Cancer*. On the other hand, exercise was not associated with prostate cancer risk among black men, or with the risk of high-grade disease, the researchers found.

Bañez and colleagues looked at results, stratified by race and exercise levels, of biopsies for 307 men suspected of prostate cancer. Exercise, assessed by a questionnaire before the procedure, was broken into 4 categories of metabolic equivalent (MET) hours per week: fewer than 3 was sedentary, 3 through 8.9 was mildly active, 9 through 17.9 was moderately active, and 18 or more was highly active.

The study cohort included 164 white men and 143 blacks, with average age of 64. There was no difference between the racial subgroups in the amount of exercise, the authors found. Biopsies found cancer in 125 men, including 54 who had high-grade disease, they reported.

Multivariate regression analysis showed that, when exercise was treated as a continuum, it did not predict a positive biopsy in the overall cohort or among the black subgroup. But among the Caucasian participants, the odds ratio for a positive biopsy was 0.90 (95% CI 0.82 to 1.00, P=0.04). In multivariate regression analysis based on different levels of exercise, using the sedentary group as a reference, Caucasian men who were at least moderately active – with more than 9 MET hours a week – had an odds ratio for a positive biopsy of 0.47 (95% CI 0.22 to 0.99, P=0.047).

Again, there was no significant benefit for any level of exercise among the black participants, Bañez and colleagues found. Among the men with cancer, they found an inverse relationship between exercise and the risk of high-grade disease (OR 0.87, P=0.01). Further analysis, as a function of race, showed that the relationship remained significant only among the white participants.

The reasons for the disparity remain unclear, although Bañez and colleagues noted there are several possible mechanisms that might play a role, including hormonal profiles and genetic susceptibilities that differ between races.

"Further studies are needed to investigate the mechanism behind this racial disparity in deriving cancer-related benefits from exercise which disfavors African American men," Bañez said in a statement.

The researchers cautioned that the cohort was small, which raises the possibility that the findings are the result of chance. In addition, factors that were not measured, such as diet, might have played a role, they added.

Bañez and colleagues also pointed out that the questionnaire, although a validated instrument did not specify the exact time frame meant by the word "current" when it asked about "current exercise," and "is therefore subject to the participant's interpretation."

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ID ERRORS IN PROSTATE BIOPSIES *(Continued from page 4)*

specimens were processed by a variety of pathology and urology laboratories.

Data for the study came from Strand Analytical Laboratories, an Indianapolis company that has developed a DNA-based test for occult SPCs. The test employs short tandem repeat (STR) analysis, originally developed by the FBI.

"STR analysis has been shown to be particularly useful in identifying occult specimen identity errors," the authors noted in their introduction.

The investigators grouped the 54 laboratories into five categories based on work flow, location, and management structure: physician-owned labs within a group-practice setting, independent reference labs, hospital labs, non-physician owned labs located in facilities shared with group practices, and labs that have the technical histopathology and professional pathology in separate facilities, necessitating transport of specimen slides.

The error rate for all labs combined was low: 0.26% for type 1 errors and 0.67% for type 2 errors. However, each SPC involved at least two patients, "the target patient and the foreign patient (or patients) whose tissue was misidentified as originating from the target patient."

Reference laboratories had the highest rate of SPCs: 0.37% for type 1 and 3.14% for type 2, resulting in an overall error rate of 3.51%.

Only 1 clinical trial has attempted to document SPCs, according to the authors. The Reduction by Dutasteride of Prostate Cancer Events (REDUCE) trial took steps to measure the rate of SPCs after 3 cases of occult biopsy specimen ID errors occurred in the first 2 years.

The rate of type 1 errors was 0.4% during the first 2 years of the REDUCE trial and declined to 0.02% in the final 2 years, after investigators implemented changes in specimen-handling procedures. A type 1 error rate of 0.5% persisted throughout the trial.

Based on their study, the authors suggested that prospective DNA testing to confirm the identity of prostate biopsies that show adenocarcinoma may be useful for preventing treatment errors stemming from misidentification.

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T2-WI & DWI MRI

(Continued from page 4)

Subgroup analysis was performed for men meeting eligibility criteria for active surveillance (AS, N=55). For this analysis, the NST group was compared to the EST/SST groups.

Results: SST status was associated with adverse preoperative risk factors for aggressive disease. Univariate analysis demonstrated significant association between SST and primary GG ≥4 pathology and stage ≥pT3 (P <0.05). On multivariate analysis, SST was independently predictive of primary GG ≥4 pathology (odds ratio [OR] 6.14, 95% confidence interval [CI] 1.97-19.2) and Gleason score (GS) upgrading (OR 2.47, 95% CI 1.01-6.02). Among men eligible for active surveillance, those in the NST group had decreased likelihood of GS ≥7 disease or stage ≥pT3 compared to the EST/SST groups (7.7% vs. 47.6%, P=0.01).

Conclusion: Increased tumor suspicion on T2-WI/DWI MRI is indicative of adverse pathology on RP. These findings suggest a role for MRI in pretreatment risk assessment.

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