Us TOO® PROSTATE CANCER EDUCATION & SUPPORT

HOTSHEET

NOVEMBER 2012

MRI HELPS IDENTIFY PATIENTS WITH PROSTATE CANCER WHO MAY BENEFIT FROM ACTIVE SURVEILLANCE

PSA screening has resulted in improved prostate cancer survival, but the high rate of diagnosis and treatment side effects raise concerns about overtreatment. Active surveillance (AS) has emerged as a plausible option to prevent overtreatment. Debate continues over the appropriate criteria for selecting men for AS. A group of investigators from Memorial Sloan-Kettering Cancer Center in New York report that adding endorectal magnetic resonance imaging (MRI) to the initial clinical evaluation of men with clinically low-risk prostate cancer helps assess eligibility for AS. Results are published in *The Journal of Urology* (Volume 188, pp.173-8, 2012).

Researchers evaluated 388 men who had an initial prostate biopsy performed between 1999 and 2010, had a Gleason score of 6 or less, and had a biopsy to confirm the assessment within 6 months of initial diagnosis. An endorectal MRI was performed in all patients between the initial and confirmatory biopsies.

MRI studies were interpreted by three radiologists with different levels of experience. Two were radiology fellows who had read about 50 and 500 previous prostate MRIs (readers 1 and 2). The third was an attending radiologist who had

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ABIRATERONE BOOSTS PROSTATE CANCER SURVIVAL

Final results of a phase III trial confirm that treatment with abiraterone prolongs overall survival (OS) in metastatic castration-resistant prostate cancer (mCRPC) that has progressed after docetaxel therapy. Over a median 20 month follow-up, median OS was 15.8 months for abiraterone (Zytiga®) plus prednisone compared with 11.2 months for placebo plus the steroid (P<0.0001), Karim Fizazi, MD, of the Institut Gustave Roussy in Villejuif, France, and colleagues reported online 18 September 2012 in *Lancet Oncology*. The findings provide "proof of principle that mCRPC remains androgen-driven," they wrote, as abiraterone is an inhibitor of CYP17 and thus suppresses androgen synthesis.

The COU-AA-301 trial enrolled 1,195 men, between 2008 and 2009, at 147 sites in 13 countries. The men had mCRPC that progressed despite docetaxel treatment. The primary endpoint was OS analyzed in the intention-to-treat population. Men were randomized to abiraterone 1,000 mg/day plus prednisone (5 mg twice a day) or to placebo plus prednisone.

An interim analysis reported a significant advantage for men taking the drug, and a data monitoring committee recommended that all participants on placebo receive abiraterone instead. The final

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STATINS DO NOT INFLUENCE BIOCHEMICAL RECURRENCE OF PROSTATE CANCER

Statins did not seem to influence the risk of biochemical recurrence (BCR) of prostate cancer after radical prostatectomy (RP) or radiotherapy (RT) results of a new meta-analysis showed.

"These results extend our 'older' meta-analysis, which had incorporated the results of six randomized clinical trials and 13 observational studies and concluded that statins do not cause any substantial change in the risk of prostate cancer," Dr. Stefanos Bonovas from University of Athens, Greece, told Reuters Health by email.

Since Dr. Bonovas's report, several additional cohort studies of statins and prostate cancer incidence were published, prompting a different team of researchers – headed by Dr. Edward Messing at the University of Rochester, NY – to perform a systematic review and meta-analysis of the observational studies with statin use as the exposure variable and biochemical failure after definitive local therapy as the outcome.

"Unfortunately, advanced prostate cancer was not a documented end-point in the randomized trials of statins," Dr. Messing and his colleagues note in their report, released online September 27 in BJU International.

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SECONDARY CANCERS AFTER INTENSITY MODULATED RADIOTHERAPY, BRACHYTHERAPY AND RADICAL PROSTATECTOMY FOR TREATMENT OF PROSTATE CANCER: INCIDENCE AND CAUSE-SPECIFIC SURVIVAL OUTCOMES ACCORDING TO THE INITIAL TREATMENT INTERVENTION

Zelefsky MJ, Pei X, Teslova T, et al

BJU Int 13 August 2012; Epub

Radiation Therapy for prostate cancer can increase the risk for the development of second cancers after treatment. This study highlights the fact that such second cancers within the pelvis do occur but are not as common as previously reported. In this report we also note that even among patients who develop second cancers, if detected earlier, the majority are alive 5 years after the diagnosis.

Objective: To report on the incidence of secondary malignancy (SM) development after external beam radiation (EBRT) and brachytherapy (BT) for prostate cancer and to compare this with a cohort contemporaneously treated with radical prostatectomy (RP).

Materials and Methods: Between 1998 and 2001, 2658 patients with localized prostate cancer were treated with RP (N = 1348), EBRT (N = 897) or BT (N = 413). Using the RP cohort as a control we compared the incidence of SMs, such as rectal or bladder cancers noted within the pelvis, and the incidence of extrapelvic SMs.

Results: The 10-year SM-free survival for the RP, BT and EBRT cohorts were 89%, 87%, and 83%, respectively (RP vs EBRT, $P = 0.002$; RP vs BT, $P = 0.37$). The 10-year likelihoods for bladder or colorectal cancer SM development in the RP, BT and EBRT groups were 3%, 2% and 4%, respectively ($P = 0.29$). Multivariate analysis of predictors for development of all SMs showed that older age ($P = 0.01$) and history of smoking ($P < 0.001$) were significant predictors for the development of a SM, while treatment intervention was not found to be a significant variable. Among 243 patients who developed a SM, the 5-year likelihood of SM-related mortality among patients with SMs in the EBRT and BT groups was 43.7% and 15.6%, respectively, compared with 26.3% in the RP cohort; $P = 0.052$).

Conclusions: The incidence of SM after radiotherapy was not significantly different from that after RP when adjusted for patient age and smoking history. The incidence of bladder and rectal cancers was low for both EBRT- and BT-treated patients. Among patients who developed a SM, the likelihood of mortality related to the SM was not significantly different among the treatment cohorts.

OBESITY PROMOTES PROSTATE CANCER BY ALTERING GENE REGULATION

Prostate cancer is one of the most common cancers in men and early treatment is usually very successful. However, like other cancers, obesity increases the risk of aggressive prostate disease. New research, published in BioMed Central's open access journal BMC Medicine, finds that the fat surrounding the prostate of overweight or obese men with prostate cancer provides a favorable environment to promote cancer growth.

Fat is a generally underrated organ. Not only is it an energy store but it secretes a wide range of growth factors, cytokines and hormones, including leptin and adiponectin, and is a major player in the immune system, which protects the body from infection and disease. But too much fat can cause these systems to go haywire and can increase risk of diabetes, cardiovascular disease and cancer.

An international team led by Prof Gema Frühbeck and Dr Ricardo Ribeiro analyzed fat, from around the prostate, taken from men undergoing surgery for prostate disease. Samples were included from men with benign prostatic hyperplasia (BPH), prostate cancer (PC), and from men whose cancer was no longer confined to the prostate. Men were also classified as being either lean (BMI<25) or overweight /obese (BMI>25).

Regardless of type of prostate disease, overweight men had different levels of gene activity in the fat surrounding their

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ABIRATERONE *(Continued from page 1)*

analysis, done before men crossed over from placebo to abiraterone and after 775 of the prespecified 797 death events, showed:

- Median OS after a median 20.2 months follow-up was significantly longer for the abiraterone versus placebo groups (HR 0.74, 95% CI 0.64 to 0.86, P <0.0001) and was consistent across all protocol-specified subgroups.
- Median time to PSA progression in abiraterone and placebo groups was 8.5 months versus 6.6 months, respectively (HR 0.63, 95% CI 0.52 to 0.78, P <0.0001)
- Median radiologic progression-free survival in abiraterone and placebo groups was 5.6 months versus 3.6 months, respectively (HR 0.66, 95% CI 0.58 to 0.76, P <0.0001)
- The proportion of men with a PSA response was 29.5% versus 5.5% in abiraterone and placebo groups, respectively (P <0.0001)

A post-hoc analysis revealed better OS with abiraterone than placebo regardless of whether it was measured from the first or last dose of docetaxel, the reason for discontinuation of docetaxel, or the time between discontinuation of docetaxel and initiation of abiraterone.

The most common grade 3-4 adverse events were fatigue, anemia, back pain, and bone pain, all occurring at similar rates in both groups, the researchers reported. But fluid retention, edema, hypokalemia, and hypertension occurred more often in the abiraterone group.

The authors acknowledged some limitations of the study, specifically that men with mCRPC and neuroendocrine differentiation, or those who previously progressed after ketoconazole treatment, were excluded from the study so the activity of abiraterone in those populations couldn't be assessed.

In an accompanying editorial, Guru Sonpavde, MD, of the University of Alabama at Birmingham, said the study "provides convincing evidence for the continued importance of androgen-axis signaling, even after chemotherapy." Yet he warned that there's little survival difference between groups at 2 years.

MedPage Today, 17 September 2012

FDA APPROVES NEW PET IMAGING AGENT FOR PROSTATE CANCER

The US Food and Drug Administration (FDA) approved the production and use of a new PET imaging agent, Choline C 11 Injection, which will be used to help detect recurrent prostate cancer.

Administered intravenously, Choline C 11 Injection produces an image that helps locate specific sites in the body for follow-up tissue sampling and testing in men with suspected recurrent disease.

The approval is limited to Choline C 11 Injection produced by the Mayo Clinic of Rochester, MN.

"Choline C 11 Injection provides an important imaging method to help detect the location of prostate cancer in patients whose blood tests suggest recurrent cancer when other imaging tests are negative," said Charles Ganley, MD, director of the Office of Drug Evaluation IV at the FDA's Center for Drug Evaluation and Research, in a statement.

The FDA's approval of Choline C 11 Injection "provides assurance to patients and health care professionals they are using a product that is safe, effective, and produced according to current good manufacturing practices," he added.

Choline C 11 Injection is a radiotracer consisting of choline labeled with the positron-emitting isotope carbon C 11. It integrates into tumor cells via an active, carrier-mediated transport mechanism for choline, according to the National Cancer Institute. The substance then undergoes intracellular phosphorylation by choline kinase, an enzyme that is often upregulated in human cancers. The end result is phosphoryl C-11 choline. Tumor cells show a higher rate of C-11 choline uptake and incorporation, as their proliferation is much higher than normal cells, thus allowing for PET imaging.

FDA confirmed the safety and effectiveness of Choline C 11 Injection by a systematic review of the published literature. The analysis included 4 independent studies, with a total cohort of 98 patients with elevated blood PSA levels but without any signs of recurrent disease or sign of recurrent prostate cancer on conventional imaging. PET imaging with Choline C 11 Injection was then

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STATINS AND BCR

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Of the eight included studies, five followed men who had RP and three followed patients after RT. Altogether they included 2,812 statin users and 10,031 nonusers. When all eight studies were considered together, there was no significant difference in the risk of BCR between statin users and nonusers, however, there was substantial evidence of heterogeneity.

Results from the RP studies were inconsistent, but overall there was no significant difference in the risk of recurrence between statin users and nonusers. Similarly, pooled results from the RT studies favored statins in a fixed effects meta-analysis but not in the random effects meta-analysis.

"Considering limitations of observational studies," researchers concluded, "it may be appropriate to investigate the effect of statins on prostate cancer recurrence and progression in randomized trials."

In the meantime, Dr. Bonovas added, "There is now accumulated evidence that statin use does not affect prostate cancer BCR. Physicians need to be vigilant in ensuring that the use of statins remains restricted to the approved cardiovascular indications."

Reuters Health, 2 October 2012

US TOO SEEKS BOARD MEMBER APPLICATIONS

Us TOO International, is seeking qualified individuals to serve on its Board of Directors. Members have been diagnosed with prostate cancer, are a member of such a man's family or significant other, or any person involved in or interested in support or treatment of such patients. Other qualifications include familiarity with an Us TOO chapter, ability to think globally, skills or experience deemed beneficial to the work of Us TOO and commitment to Us TOO's purpose and mission.

See details at www.ustoo.org/SeekBoardMembers.asp. Send letters of nomination with a vita or resume to Thomas Kirk, President and CEO, Us TOO International, 5003 Fairview Avenue, Downers Grove, IL 60515 or e-mail tom@ustoo.org.

18F-FLUOROETHYLCHOLINE PET/CT IDENTIFIES LYMPH NODE METASTASIS IN PATIENTS WITH PROSTATE-SPECIFIC ANTIGEN FAILURE AFTER RADICAL PROSTATECTOMY BUT UNDERESTIMATES ITS EXTENT

Tilki D, Reich O, Graser A, et al

Eur Urol, 10 August 2012; Epub

Background: The detection of lymph node metastases (LNMs) is one of the biggest challenges in imaging in urology.

Objective: To evaluate the accuracy of combined 18F-fluoroethylcholine (FEC) positron emission tomography (PET)/ computed tomography (CT) in the detection of LNMs in prostate cancer patients with rising PSA level after radical prostatectomy.

Design, Settings, and Participants: From June 2005 until November 2011, 56 prostate cancer patients with biochemical recurrence after radical prostatectomy underwent bilateral pelvic and/or retroperitoneal lymphadenectomy based on a positive 18F-FEC PET/CT scan.

Outcome Measurements and Statistical Analysis: The findings of PET/CT were compared with histologic results.

Results and Limitations: Median PSA value at the time of 18F-FEC PET/CT analysis was 6.0 ng/ml (interquartile range: 1.7-9.4 ng/mL). In 48 of 56 (85.7%) patients with positive 18F-FEC PET/CT findings, histologic examination confirmed the presence of prostate cancer in LNMs. Of 1149 lymph nodes that were removed and histologically evaluated, 282 (24.5%) harbored metastasis. The mean number of lymph nodes removed per surgical procedure was 21 (SD ±18.3). A lesion-based analysis yielded 18F-FEC PET/CT sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 39.7%, 95.8%, 75.7%, and 83.0%, respectively. A site-based analysis yielded sensitivity, specificity, PPV, and NPV of 68.4%, 73.3%, 81.3%, and 57.9%, respectively. Patients with negative PET/CT did not undergo surgery, thus sensitivity, specificity, and negative predictive value on a patient basis could not be calculated.

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NO QUALITY OF LIFE HIT WITH LONG-TERM FINASTERIDE

Finasteride therapy for as long as 7 years had only a minor impact on physical function, accounting for less than a one-point decrement over time, beginning 3 months before initiation of therapy. Similarly, long-term treatment with the drug had no impact on mental health or vitality. Comorbidities, such as congestive heart failure (CHF) and diabetes, did have statistically significant negative effects on physical function, as reported online in the *Journal of the National Cancer Institute*.

The Prostate Cancer Prevention Trial (PCPT) afforded greater opportunity to examine the effects of long-term finasteride therapy on more general aspects of health and quality of life. The PCPT involved 18,882 middle-age and older men who were randomized to finasteride or placebo and followed for 7 years to determine whether daily finasteride reduced the risk of prostate cancer in average-risk men. The primary outcome was prostate cancer incidence, which was about 25% lower in the finasteride arm.

Carol M. Moinpour PhD, of Fred Hutchinson Cancer Research Center in Seattle, and co-authors from the PCPT prospectively assessed QoL in study participants, beginning 3 months before randomization and continuing on a regular basis until the trial ended. Those data provided a unique opportunity to study the effects of long-term finasteride on health-related QoL, they stated.

The initial report from the trial only reported problems with sexual function. However, other aspects of health-related QoL had not been examined in detail. Health-related QoL was a prespecified secondary endpoint of the PCPT and was measured by means of the Short Form 36 questionnaire (SF-36). The SF-36 permits quantification of changes in 8 scales related to physical and mental health.

Moinpour and co-authors limited their analysis to PCPT participants who completed the SF-36 at least twice after randomization. The restriction resulted in a study population of 16,077 men. The investigators also limited the analysis to 3 domains of the SF-36: physical functioning, mental health, and vitality.

The primary finding was that treatment with finasteride for as long as 7 years did not have a significant adverse effect on the three domains assessed. For physical functioning, calculations resulted in a mixed-effect estimate of 0.07, associated with a *P* value of 0.71.

Similar results emerged from analyses of mental health and vitality. In contrast, several comorbid conditions significantly affected physical functioning, e.g., CHF (-5.64), diabetes (-1.31) and leg pain (-2.57), all $P < 0.001$. Current smoking also affected physical health adversely (mixed-effects estimate = -2.34, $P<0.001$).

"Our results show that natural sources of variability in the heterogeneous population and comorbidity status at study entry, particularly diabetes and current smoking status, had a greater clinically relevant impact on the Physical Functioning score than did finasteride treatment," Carol M. Moinpour PhD, of Fred Hutchinson Cancer Research Center in Seattle, and co-authors wrote in conclusion.

"Our findings reinforce the need to consider individual differences in age, time on study, smoking status, and medical comorbidities when evaluating the effect of different preventive interventions on health-related quality of life."

Information about finasteride's impact on health-related quality of life has come largely from clinical research on two conditions: benign prostatic hyperplasia (BPH) and alopecia. Clinical trials in those two areas, particularly BPH, tended to focus on disease-specific symptoms.

"Taken altogether ... our results indicate that finasteride is a low-risk preventative agent with minimal impact on health-related quality of life," the authors wrote.

MedPage Today, 13 September 2012

C11 CHOLINE FDA APPROVED

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performed, and patients who had abnormalities detected on PET scanning underwent tissue biopsy.

In each of these studies, at least half of the patients who had abnormalities detected on PET scanning with the new agent also were confirmed to have recurrent prostate cancer, after pathology testing of the abnormal tissue.

However, PET scan errors also were reported. Although it varied across studies, false-positive PET scans were observed in 15% to 47% of patients, thus underscoring the necessity for confirmatory tissue biopsy.

According to the FDA, Choline C 11 Injection must be produced in a specialized facility and administered to patients soon after it is produced. Although PET imaging with Choline C 11 Injection has been used at several institutions during the past few years, none have been approved by the FDA to manufacture the agent. The Mayo Clinic PET Radiochemistry Facility is the first FDA-approved facility for the production of Choline C 11 Injection.

The Mayo Clinic has conducted studies with Choline C 11 Injection, 3 of which were presented at the 2012 annual meeting of the American Urological Association. "Taken together, the three studies represent an important validation of the C-11 choline PET/CT scan as an evaluation tool for patients with prostate cancer," said Jeffrey Karnes, MD, from the Mayo Clinic and senior author of all 3 papers, in a press release. "We believe the use of these scans can improve the evaluation and treatment of this common form of cancer, while potentially reducing the cost of delivering the best possible care."

Uncommon mild skin reactions at the injection site were the only adverse effect attributed to the use of the agent.

Medscape, 2 October 2012

MRI HELPS IDENTIFY AS CANDIDATES

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interpreted over 5,000 prostate MRI examinations (reader 3). They each assigned a score of 1 to 5 for the presence of tumor on MRI, with 1 being definitely no tumor and 5 being definitely tumor.

On confirmatory biopsy, Gleason scores were upgraded in 79 (20%) cases. An MRI score ≤2 was highly associated with low risk features on confirmatory biopsy. Agreement on MRI scores was substantial between readers 2 and 3, but only fair between reader 1 and readers 2 and 3. Results suggest that MRI of the prostate, if read by radiologists with appropriate training and experience, could help determine AS eligibility.

"Among men initially diagnosed with clinically low risk prostate cancer, those with tumors not clearly visualized on MRI were significantly more likely to demonstrate low risk features when a confirmatory biopsy was performed, while men with clearly visualized tumors were significantly more likely to have their disease status upgraded on confirmatory biopsy," concluded lead investigator Hebert Alberto Vargas, MD, Department of Radiology, Memorial Sloan-Kettering Cancer Center.

In an editorial, Guillaume Ploussard, MD, PhD, of the CHU Saint-Louis, APHP, Paris, France, notes "The primary issue is to reduce the number of clinical settings in which the urologist and the patient face the situation of an increased PSA and an uncertain diagnosis. MRI might help to limit the risk of biopsy under-grading. In cases of normal signal in the whole gland, the patient might be reassured and re-biopsy delayed. In cases of a suspicious nodule, re-biopsy would be better justified, and biopsy cores could target specific zones."

Elsevier company news, 24 September 2012

ASK DOCTOR SNUFFY MYERS

In July 2007 at age 70, I was diagnosed with 3+3 Gleason prostate cancer and underwent radioactive seed implantation in January 2008. In 2009, I was diagnosed with bladder neck contracture and have undergone several procedures to resolve this. I had a "mini-TURP" in May 2009, hyperbaric oxygen treatments in November 2009, TURBN in December 2009 and had a vesical neck contracture dilated in December 2010 and again in November 2011. My urologist recommends conservative management using intermittent self-catheterization instead of further procedures that could result in incontinence. I now self-catheterize once daily (previously 3 times a day). Despite this, I develop urinary retention every few months. My question: are there any procedures that could possibly correct my situation "permanently" with minimal risk of incontinence? I still work and have a very active lifestyle and I don't want to compromise that. Also, what is the likelihood of incontinence if I decide to be more aggressive? I am getting very impatient and discouraged with my current situation. I appreciate whatever advice you can provide and please feel free to publish this information.

With your initial findings, you should never have had brachytherapy. This is yet another case of needless overdiagnosis and overtreatment. Unfortunately, you are experiencing severe complications from this needless treatment. I do not understand why you were given hyperbaric oxygen. It is used to treat radiation-induced bleeding from the bladder or bowel, but has no impact at all on the fibrosis.

There are two randomized controlled trials showing that Trental® and vitamin E reduce radiation scarring and that would be a place to start. Unfortunately, not everyone responds to this and it is uncommon to get complete resolution of scaring with this approach.

A class of drugs used to treat high blood pressure also lessen scarring at many sites. Angiotensin receptor blockers have been shown to decrease scarring in the heart and blood vessels. Several clinical trials have shown a favorable impact on radiation damage. Losartan is one member of this class and is now generic. We would commonly add losartan to Trental® and vitamin E.

After radiation, I had problems with scarring in the muscles of my hip. At one point, I was not able to bend over and tie my shoelaces. Trental, vitamin E and losartan reversed that problem.

DIRECT 2-ARM COMPARISON SHOWS BENEFIT OF HIGH-DOSE-RATE BRACHYTHERAPY BOOST VS EXTERNAL BEAM RADIATION THERAPY ALONE FOR PROSTATE CANCER

Khor R, Duchesne G, Tai KH, et al

Int J Radiat Oncol Biol Phys
3 September 2012; Epub

Purpose: To evaluate the outcomes of patients treated for intermediate- and high-risk prostate cancer with a single schedule of either external beam radiation therapy (EBRT) and high-dose-rate brachytherapy (HDRB) boost or EBRT alone.

Methods and Materials: From 2001-2006, 344 patients received EBRT with HDRB boost for definitive treatment of intermediate- or high-risk prostate cancer. The prescribed EBRT dose was 46 Gy in 23 fractions, with a HDR boost of 19.5 Gy in 3 fractions. This cohort was compared to a contemporaneously treated cohort who received EBRT to 74 Gy in 37 fractions, using a matched pair analysis. Three-dimensional conformal EBRT was used. Matching was performed using a propensity score matching technique. High-risk patients constituted 41% of the matched cohorts. Five-year clinical and biochemical outcomes were analyzed.

Results: Initial significant differences in prognostic indicators between the unmatched treatment cohorts were rendered negligible after matching, providing a total of 688 patients. Median biochemical follow-up was 60.5 months. The 5-year freedom from biochemical failure was 79.8% (95% confidence interval [CI], 74.3%-85.0%) and 70.9% (95% CI, 65.4%-76.0%) for the HDRB and EBRT groups, respectively, equating to a hazard ratio of 0.59 (95% CI, 0.43-0.81, $P = 0.0011$). Interaction analyses showed no alteration in HDR efficacy when planned androgen deprivation therapy was administered (P = 0.95), but a strong trend toward reduced efficacy was shown compared to EBRT in high-risk cases ($P = 0.06$). Rates of grade 3 urethral stricture were 0.3% (95% CI, 0%-0.9%) and 11.8% (95% CI, 8.1%-16.5%) for EBRT and HDRB,

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

"Can improving your "core" reduce side effects from prostate cancer treatment? Yes!"

Mark A. Moyad, MD, MPH
University 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.

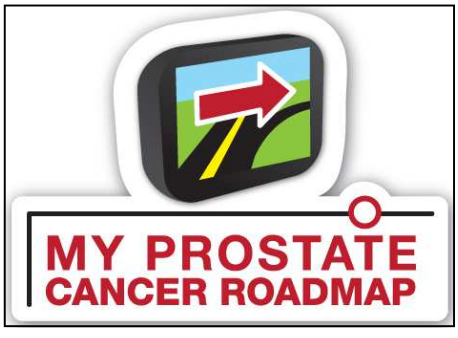
Bottom Line: A new randomized trial of men after prostate cancer surgery suggests that doing more than just Kegel exercises can dramatically improve urinary and physical function and quality of life, so how groovy is that (1970s endearing term that I still like to use).[1] Oh, and go out and learn to do "core" exercises with the use of a "balance ball" please!

This was a randomized trial of 66 patients allocated to a combined (resistance, flexibility, and Kegel) "core" exercise or control group (only Kegel). The intervention was conducted twice a week for 12 weeks beginning at post-op week 3. The average age and BMI (body mass index) was 69 years and 24 (normal weight). The continence rate in the exercise group was 73% versus 44% in the control group after the 12 weeks, and the 24-hour incontinence pad test also demonstrated significantly better results with "core" exercises. After 12-weeks basically all physical functions (fitness, flexibility, and balance) were significantly better in the exercise versus the control group. Only the exercise group experienced significant improvements in qualify of life, including reduced depression scores based on a series of questionnaires. No changes were observed in fat mass, muscle mass, BMI or waist/hip ratio after the exercise intervention (in other words this is what we call "low impact" core exercises-perfect after treatment).

Wow! My personal bias is that if patients would have continued to do these exercises for 1-year it would probably also further improve continence and even erectile function rates. The greater lesson here is that I believe I (along with some of my urologic colleagues) have in the past "ignored the core" (sorry I just trademarked that phrase) so to speak. We can get so excited recommending lifestyle and dietary changes and even resistance exercises but in reality the abdomen, pelvis and back muscle areas really appear to get ignored apart from the ageless, timeless, and effortless Kegel exercises. Can't we do better than just Kegel exercises after all these decades of surgery and radiation being a primary treatment for prostate cancer (rhetorical Moyad moment)? Sure, I curse the men and women on the cover of the fitness and muscle magazines because of their 6-pack abs that I know I could never achieve without some photographic airbrushing expert(s) or plastic surgeon, or 20-hour a day/7-day a week workouts that must involve quitting my job and having no life whatsoever! Yet, perhaps many of the yoga and Pilates "core" exercise group advocates have been right all along and we have been wrong. I really believe that this research has changed my perspective on the importance of working on "core strengthening" exercises so that all muscle groups have balanced strength and benefit. Move over Kegel, there is a new sheriff in town and his name is "core", and he/she believes that working with a balance ball and doing a variety of core exercises can change your life and make you look even sexier than you look right now (that is pretty darn sexy). Talk to a trainer, sign up for a class, or look on the internet for low impact "core strengthening" exercises using a balance ball or pick up a future Moyad book (how about that for a shameless plug).

Reference

1. Park SW, Kim TN, Nam JK, et al. *Urology* 2012; 80: 299-306.



DOCTOR CHODAK'S BOTTOM LINE *(Ref Key: article #, page #, column #)*

Editor: www.prostatevideos.com

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.

a1p1c1 As more doctors recognize that the overdetection of prostate cancer is a problem, they are increasingly searching for ways to distinguish those cancers needing treatment from those that might be observed. MRI may offer an option for helping with this problem. The study by Vargas found that men with a not-suspicious MRI for cancer more often were found to have low risk disease. Further studies are needed, however, to prove that the accuracy is sufficient and variability in the experience of radiologists could impact on the overall results.

The Bottom Line: MRI might become a useful tool for men with low risk cancer who are candidates for active surveillance.

a2p1c2 More data is now available on abiraterone acetate showing two important results. First it further demonstrates the ability of this drug to improve survival in men failing docetaxel chemotherapy, and second, it shows that even when men progress following castration, they still can respond to further reductions in testosterone. Certainly, this is not a home run, meaning that men still die of their disease, although they survive for a longer time. Preliminary results have already shown that men can gain an even greater benefit by receiving abiraterone prior to chemotherapy. This raises the question as to whether using it even earlier in the disease, possibly instead of an LHRH medication, can deliver even better results.

The Bottom Line: Abiraterone improves survival for men with progressive metastatic prostate cancer and the benefit increases as treatment is delivered earlier in the course of metastatic disease.

a3p1c3 Conflicting results have been reported on the impact of statins in men with prostate cancer although none of them were randomized studies. Another analysis by Messing and his colleagues comes to the conclusion that statin users were not less likely to develop disease progression after radical prostatectomy (RP) or radiation therapy (RT) compared to non-users but we are left asking whether we can truly make any better conclusions from this study than previous ones.

The Bottom Line: Until we have data from a randomized study, the true value of statins in men with prostate cancer will remain unknown. For now, these drugs should only be taken for the indications approved by the FDA.

a4p2c2 Does RT increase a man's risk of developing rectal or bladder cancer? This question has never been fully evaluated. Assessments from large data bases suggest an incidence of these cancers of 1-3% but it may take 15 years to be identified. The study by Zelefsky on a modest size cohort suggested that there is no added risk but the study has some weaknesses. It is unclear how many men were lost to follow-up or died before 10 years. Also, the analysis may be premature with none followed for a minimum of 15 years.

The Bottom Line: Population data suggest that pelvic RT for prostate cancer does lead to a slight increase in the risk of rectal or bladder cancer but it may not occur for more than ten years. This risk may increase, however, now that men are getting treated at an earlier age with higher doses of RT and in some cases using higher fractionations but more time will be needed to fully assess this risk.

a6p4c1 The report on detecting lymph nodes using ^{18}F-fluorethylcholine PET/CT scans provides some interesting information and also raises questions. Men with a rising PSA after RP underwent this test prior to a lymphadenectomy. Nearly one-quarter of the men were found to have lymph node metastases at RP. The PET/CT scan was falsely positive in about 25% and falsely negative in 17%. Many questions are raised by these results such as:

- Why did these men not have their lymph nodes removed during the RP?
- How did the clinicians justify removing the lymph nodes at a second operation when there is no proof that it would improve survival?
- How many men could have been detected by a simple CAT scan or MRI rather than by the PET scan?

Eventually with more data, this test might have value in deciding who should avoid either surgery or radiation because they already harbor metastases in their lymph nodes. Before that can occur, much more data are needed.

The Bottom Line: PET/CT scans for evaluating pelvic lymph nodes may have some merit for planning proper therapy but more studies are needed before that can occur.

a9p6c1 Another ongoing controversy for managing intermediate and high-risk prostate cancer is the role of HDR (high-dose rate brachytherapy) in addition to external beam RT (EBRT). The study by Khor and co-workers attempts to compare EBRT alone to EBRT with 3 fractions of HDR. The results suggest a lower risk of biochemical failure (BCR) at 5 years using the combination treatment; however, the trade-off is a much higher risk of grade 3 urethral strictures. The study suffers from several weaknesses. Of course the most important is that the study is not randomized and consequently is subject to all of the limitations that go along with this study design. Also, since randomized studies have proven a survival benefit by combining androgen deprivation therapy (ADT) with EBRT, it is unclear how often that was utilized in the men treated with EBRT without HDR and how it might have impacted on the results. Lastly, BCR is not an adequate measure of the effectiveness of RT because it does not always directly correlate with survival.

The Bottom Line: Without proper studies, men should not be advised to have HDR added to EBRT especially because it has a higher complication rate. A safer and more appropriate treatment would be EBRT combined with ADT.

PET/CT AND LYMPH NODES

(Continued from page 4)

Conclusions: A positive 18F-FEC PET/CT result correctly predicted the presence of LNM in the majority of prostate cancer patients with biochemical failure after radical prostatectomy but did not allow for localization of all metastatic lymph nodes and therefore was not adequately accurate for the precise estimation of extent of nodal recurrence in these patients.

EBRT VS EBRT + BT BOOST

(Continued from page 6)

respectively (P <0.0001). No differences in clinical outcomes were observed.

Conclusions: This comparison of 2 individual contemporaneously treated HDRB and EBRT approaches showed improved freedom from biochemical progression with the HDBR approach. The benefit was more pronounced in intermediate- risk patients but needs to be weighed against an increased risk of urethral toxicity.

OBESITY AND GENES

(Continued from page 2)

prostates compared to the lean men. This included genes which encode proteins involved in immunity and inflammation (such as LEP, which encodes the protein leptin), and cell growth and proliferation (including ANGPT1 which encodes angiopoietin 1), fat metabolism and programmed cell death.

Additionally the activity of more genes was altered between hyperplasia and prostate cancer, and between cancer and non-confined cancer, suggesting a gradual increase in dysregulation during cancer progression.

Prof Frühbeck explained, "Both LEP and ANGPT1 encode proteins which are thought to have roles beyond adipose tissue itself, especially because prostate cancer cells have receptors for leptin, and angiopoietin 1. Taken together with the abnormal activity levels of other genes they will ultimately foster fat mass growth, reduce immune surveillance, and promote the formation of new blood vessels, so producing a favorable environment for prostate cancer progression."

Dr Ribeiro continued, "In an increasingly obese population, understanding how fat, especially the fat surrounding the prostate, can influence the growth and severity of prostate cancer may provide an opportunity for implementing personalized lifestyle and therapeutic strategies."

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