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NEW RADIOTRACER FOR PROSTATE CANCER SHOWS PROMISE

A new radiotracing agent injected before PET/CT might improve the detection of metastasized prostate cancer, compared with conventional imaging, in men with castration-resistant prostate cancer (CRPC), according to preliminary results from a new study.

The agent, known as 18F-DCFBC, binds to prostate-specific membrane antigen (PSMA), a protein that is "highly expressed in prostate cancer, allowing for optimal signal detection," said senior author Steve Cho, MD, PhD, from Johns Hopkins University School of Medicine in Baltimore, Maryland.

"The new findings, presented here at the Society of Nuclear Medicine and Molecular Imaging (SNMMI) 2014 Annual Meeting, confirm the tracer's reliability for detecting prostate cancer, regardless of androgen or serum folate levels," said Steven Rowe, MD, PhD, also from Johns Hopkins, who presented the results.

"We were able to detect lymph node, bone, and visceral metastases in both castration-sensitive and castration-resistant prostate cancer," he reported. And there was "no evidence of uptake inhibition by high serum folate levels." The uptake of 18F-DCFBC "correlated fairly well with conventional imaging, but we saw more lesions," said Dr. Cho.

The study is ongoing, but preliminary results are available for 12 men with metastatic prostate cancer. The median age was 69 years and median PSA level

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HOTSHEET

AUGUST 2014

SLOW GROWTH FOR ACTIVE SURVEILLANCE IN PROSTATE CANCER

Use of active surveillance (AS) for localized prostate cancer varied substantially by demographics and geography, in addition to disease characteristics, according to an analysis of Medicare data.

From 2004 to 2007, use of AS versus watchful waiting increased from 9.7 percent to 15.3 percent ($P < 0.001$). Increased use of AS was associated with higher socioeconomic status (SES) and white race, investigators reported in the July issue of *The Journal of Urology*. Older age, comorbidities, and high-risk tumor characteristics were associated with a reduced likelihood that a man would enter AS.

Christopher P. Filson, MD, of the University of California Los Angeles, and co-authors reported that, geographically, use of AS ranged from 2.4 to 30.1 percent with no clear association to specific healthcare market characteristics.

As a result of widespread use of PSA screening tests, the vast majority of newly diagnosed prostate cancers are early-stage, localized disease. Though some of the men will benefit from immediate treatment, most of the cancers are not life threatening.

In response to concerns about overtreatment of prostate cancer, many medical centers have established AS protocols to distinguish between indolent and clinically significant cancers. Since no standard protocol exists, clinical guidelines provide limited direction for patient

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CHANGES IN SEXUAL ROLES AND QUALITY OF LIFE FOR GAY MEN AFTER PROSTATE CANCER: CHALLENGES FOR SEXUAL HEALTH PROVIDERS

Hart T, Coon D, Kowalkowski M, et al
J Sex Med 30 May 2014; Epub

Introduction: Gay men with prostate cancer (GMPc) may have differential health-related quality of life (HRQOL) and sexual health outcomes than heterosexual men with prostate cancer (PCa), but existing information is based on clinical experience and small studies.

Aims: Our goals were to: (i) describe HRQOL and examine changes in sexual functioning and bother; (ii) explore the psychosocial aspects of sexual health after PCa; and (iii) examine whether there were significant differences on HRQOL and sexual behavior between GMPc and published norms.

Methods: A convenience sample of GMPc completed validated disease-specific and general measures of HRQOL, ejaculatory function and bother, fear of cancer recurrence, and satisfaction with prostate cancer care. Measures of self-efficacy for PCa management, illness intrusiveness, and disclosure of sexual orientation were also completed. Where possible, scores were compared against published norms.

Main Outcome Measures: Main outcome measures were self-reported sexual functioning and bother on the Expanded Prostate Cancer Index.

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COMPARATIVE EFFECTIVENESS OF AGGRESSIVE VERSUS NONAGGRESSIVE TREATMENT AMONG MEN WITH EARLY-STAGE PROSTATE CANCER AND DIFFERING COMORBID DISEASE BURDENS AT DIAGNOSIS

Daskivich TJ, Lai J, Dick AW, et al
Cancer 13 May 2014; Epub

Background: This study sought to compare the effectiveness of aggressive versus nonaggressive treatment in reducing cancer-specific mortality (CCM) for older men with early-stage prostate cancer across differing comorbid disease burdens at diagnosis.

Methods: In total, the authors sampled 140,553 men aged ≥ 66 years with early-stage prostate cancer who were diagnosed between 1991 and 2007 from the Surveillance, Epidemiology, and End Results-Medicare database. Propensity-adjusted competing-risks regression analysis was used to compare the risk of CCM between men who received aggressive versus nonaggressive treatment among comorbidity subgroups.

Results: In propensity-adjusted competing-risks regression analysis, aggressive treatment was associated with a significantly lower risk of CCM among men who had Charlson scores of 0, 1, and 2 but not among men who had Charlson scores ≥ 3 (subhazard ratio, 0.85; 95% confidence interval, 0.62-1.18). The absolute reduction in 15-year CCM between men who received aggressive versus nonaggressive treatment was 6.1%, 4.3%, 3.9%, and 0.9% for men with Charlson scores of 0, 1, 2, and ≥ 3 , respectively. Among men who had well-differentiated and moderately-differentiated tumors, aggressive treatment again was associated with a lower risk of CCM for those who had Charlson scores of 0, 1, and 2 but not for those who had Charlson scores ≥ 3 (subhazard ratio, 1.14; 95% confidence interval, 0.70-1.89). The absolute reduction in 15-year CCM between men who received aggressive versus nonaggressive treatment was 3.8%, 3%, 1.9%, and -0.5% for men with Charlson scores of 0, 1, 2, and ≥ 3 , respectively.

Conclusions: The cancer-specific survival benefit from aggressive treatment for early-stage prostate cancer diminishes with increasing comorbidity at diagnosis. Men with Charlson scores ≥ 3 garner no survival benefit from aggressive treatment.

COMPARING 3T MULTIPARAMETRIC MRI AND THE PARTIN TABLES TO PREDICT ORGAN-CONFINED PROSTATE CANCER AFTER RADICAL PROSTATECTOMY

Gupta RT, Faridi KF, Singh AA, et al
Urol Oncol 23 May 2014; Epub

Objectives: The purpose of our study was to test our hypothesis that multiparametric magnetic resonance imaging (mpMRI) may have a higher prognostic accuracy than the Partin tables in predicting organ-confined (OC) prostate cancer and extracapsular extension (ECE) after radical prostatectomy (RP).

Methods and Materials: After institutional review board approval, we retrospectively reviewed 60 men who underwent 3T mpMRI before RP. MpMRI was used to assess clinical stage and the updated version of the Partin tables was used to calculate the probability of each man to harbor OC disease (OCD). Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of mpMRI in detecting OC and ECE were calculated. Logistic regression models predicting OC pathology were created using either clinical stage at mpMRI or Partin tables' probability. The area under the curve (AUC) was used to calculate the predictive accuracy of each model.

Results: Median PSA level at diagnosis was 5ng/mL (range: 4.1-6.7ng/mL). Overall, 52 (86.7%) men had cT1 disease, seven (11.7%) had cT2a/b, and one (1.6%) had cT3b at digital rectal examination. Biopsy Gleason score was 6, 3+4=7, 4+3=7, 8, and 9-10 in 28 (46.7%), 15 (25%), three (5%), 10 (16.7%), and four (6.6%) men, respectively. At mpMRI, clinical stage was defined as cT2a/b, cT2c, cT3a, and cT3b in 11 (18.3%), 23 (38.3%), 21 (35%), and five (8.4%) men, respectively. At final pathology, 38 men (63.3%) had OCD, whereas 18 (30%) had ECE and four (6.7%) had seminal vesicle invasion. The sensitivity, specificity, PPV, and NPV of mpMRI in detecting OCD were 81.6%, 86.4%, 91.2%, and 73.1%, respectively, whereas in detecting ECE were 77.8%, 83.4%, 66.7%, and 89.7%, respectively.

At logistic regression, both the Partin tables-derived probability and the mpMRI clinical staging were significantly associated with OCD (all $P < 0.01$). The AUCs of the model built us-

(Continued on page 3)

CONCERN FOR OVERTREATMENT USING THE AUA/ASTRO GUIDELINE ON ADJUVANT RADIOTHERAPY AFTER RADICAL PROSTATECTOMY

Kang JH, Ha Y-S, Kim S, et al
BMC Urol 2014; 14(30) [proof]

Background: Recently, three prospective randomized trials have shown that adjuvant radiotherapy (ART) after radical prostatectomy (RP) for men with pT3 and/or positive margins improves biochemical progression-free survival and local recurrence-free survival. But, the optimal management of these patients after RP is an issue which has been debated continuously. The object of this study was to determine the necessity of ART by reviewing the outcomes of observation without ART after RP in men with pathologic indications for ART according to the current American Urological Association (AUA)/ American Society for Radiation Oncology (ASTRO) guideline.

Methods: From a prospectively maintained database, 163 men were eligible for inclusion in this study. These men had a pathological stage pT2–3 N0 with an undetectable PSA level after RP and met one or more of the three following risk factors: capsular perforation, positive surgical margins, or seminal vesicle invasion. We excluded the men who had received neoadjuvant hormonal therapy or adjuvant treatment, or had less than 24 months of follow-up. To determine the factors that influenced biochemical recurrence (BCR)-free, univariate and multivariate Cox proportional hazards analyses were performed.

Results: Among the 163 men, median follow-up was 50.5 months (24.0–88.2 months). Of those men under observation, 27 had BCR and received salvage radiotherapy (SRT). The multivariate Cox analysis showed that BCR was marginally associated with pre-operative serum PSA ($P = 0.082$), and the pathologic GS (HR, 4.063; $P = 0.001$) was an independent predictor of BCR. More importantly, in 87 men with pre-RP PSA <6.35 ng/ml and GS ≤ 7 , only 3 developed BCR.

Conclusions: Of the 163 men who qualified for ART based on the current AUA/ASTRO guideline, only 27 (16.6%) developed BCR and received SRT. Therefore, using ART following RP using the current recommendation may be an overtreatment in an overwhelming majority of the patients.

IMPACT OF NADIA PROSVUE PSA SLOPE ON SECONDARY TREATMENT DECISIONS AFTER RADICAL PROSTATECTOMY

Moul JW, Chen DYT, Trabulsi EJ, et al
Prostate Cancer Prostatic Dis 15 July 2014; Epub

Background: Selecting appropriate candidates for postprostatectomy radiotherapy is challenging because adverse pathologic features cannot accurately predict clinical recurrence. Biomarkers that identify residual disease activity may assist clinicians when counseling patients on the risks, benefits and costs of secondary treatment. NADiA® ProsVue™ PSA slope results ≤ 2.0 pg/mL/mo are predictive of a reduced risk of clinical recurrence, however, its clinical utility has not yet been studied.

Methods: We prospectively enrolled men treated by radical prostatectomy in a multicenter, IRB-approved clinical trial. At post-surgical followup, investigators ($N=17$) stratified men into low-, intermediate- or high-risk groups for prostate cancer recurrence based on clinicopathologic findings and other factors. Investigators documented their initial treatment plan for each subject and serially collected three serum samples for ProsVue testing. After the ProsVue result was reported, investigators recorded whether or not the initial treatment plan was changed. The proportion of cases referred for secondary treatment before and after ProsVue was reported and the significance of the difference determined.

Results: Complete assessments were reported for 225 men, 128 (56.9%) of whom were stratified into intermediate and high risk groups. Investigators reported that they would have referred 41/128 (32.0%) at-risk men for secondary treatment. However, after results were known, they referred only 15/128 (11.7%) men. The difference in proportions (-20.3%, 95% confidence interval [CI] -29.9 to -10.3%) is significant ($p < 0.0001$). Odds of a referral was significantly reduced after results were reported (Odds Ratio 0.28, 95% CI 0.15–0.54, $p < 0.0001$).

Conclusion: Knowledge of a ProsVue result had significant impact on the final treatment plan. A ProsVue result ≤ 2.0 pg/mL/mo significantly reduced the proportion of men at risk of recurrence that would otherwise have been referred for secondary treatment.

SLOW GROWTH FOR AS

(Continued from page 1)

selection, and use of AS remain poorly understood because fewer than 10 percent of men enrolled in protocols prior to 2007.

To examine trends in active surveillance, Filson and colleagues analyzed Medicare-linked data from the National Cancer Institute's Surveillance, Epidemiology and End Results program for the years 2004 to 2007. They identified all patients who did not have definitive treatment within 12 months of diagnosis (expectant treatment) and evaluated factors associated with use of AS (repeat biopsy and PSA testing) versus watchful waiting.

The query identified 7,347 men ≥ 66 with expectantly managed prostate cancer during the study period. Overall, 932 (12.4%) entered AS. The authors found that use of AS decreased with increasing patient age ($P < 0.001$ for trend), number of comorbid conditions ($P < 0.001$), and tumor risk ($P < 0.001$).

Use of AS increased with SES ($P < 0.001$) and was more common in white men (13%) as compared with black men (11.2%) or "other" (10.2%). Although use of AS varied significantly by geography, the authors could find no market-specific characteristics associated with AS.

The authors concluded that future research should seek to quantify patient and provider contributions to the variation, identify facilitators and barriers to use of AS, identify factors associated with racial variations, and use other data sources to improve understanding of variations in use of AS across insurance plans and age groups.

MedPage Today, 2 July 2014

MpMRI VERSUS PARTIN TABLES

(Continued from page 2)

ing the Partin tables and that of the mpMRI model were 0.62 and 0.82, respectively ($P = 0.04$).

Conclusions: The predictive accuracy of mpMRI in predicting OCD on pathological analysis is significantly greater than that of the Partin tables. MpMRI had a high PPV (91.2%) when predicting OCD and a high NPV (89.7%) with regards to ECE. MpMRI should be considered when planning prostate cancer treatment in addition to readily available clinical parameters.

LOW DETECTABLE PSA AFTER RADICAL PROSTATECTOMY: TREAT OR WATCH?

Koulikov D, Mohler M, Mehedint D, et al

J Urol 21 May 2014; Epub

Purpose: To determine whether the pattern of low detectable prostate-specific antigen (PSA) during the first three years of follow-up after radical prostatectomy is a predictor for subsequent biochemical recurrence.

Materials and Methods: An institutional database was queried to identify 1,136 men who underwent open retropubic radical prostatectomy or robot-assisted radical prostatectomy 1/5/1993 - 12/29/2008. After applying exclusion criteria, serum PSA and pattern during the first 3 years of follow-up were used to separate 566 men into 3 groups: 1) undetectable PSA (PSA \leq 0.03 ng/mL); 2) low detectable stable PSA (PSA $>$ 0.03 and $<$ 0.2 ng/mL; no two subsequent increases and/or PSA velocity (PSAV) $<$ 0.05 ng/year); 3) low detectable unstable PSA (PSA $>$ 0.03 and $<$ 0.2 ng/mL; two subsequent increases (National Comprehensive Cancer Network [NCCN]) and/or PSAV \geq 0.05 ng/year). The primary end point was biochemical recurrence, which was defined as PSA \geq 0.2 ng/mL or receipt of radiation therapy beyond 3 years of follow-up.

Results: 7-year biochemical recurrence-free survival was 95%, 94%, and 37% for the undetectable, low detectable-Stable, and low detectable-Unstable groups, respectively (Log-rank test, $p <$ 0.0001). On multivariate analyses, the PSA pattern during the three years after operation (undetectable versus low detectable-Unstable, HR=15.9; undetectable versus low detectable-Stable, HR=1.6), pathological T (pT2 versus $>$ pT2, HR=1.8), pathological Gleason score ($<$ 7 versus 7, HR=2.3; $<$ 7 versus 8-10, HR=3.3) and surgical margins (negative versus positive, HR=1.8) significantly predicted biochemical recurrence.

Conclusion: The combination of PSAV and NCCN criteria for biochemical recurrence following radical prostatectomy separated well men with low detectable PSA after RP into those who require treatment from those who can be watched safely.

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

"Breaking news on vitamin C and E dietary supplements and cancer? Nada!"

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

Editor's 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:

In one of the largest randomized trials (PHS2) to determine the impact of vitamin C (500 mg every day) and vitamin E (400 IU dl-alpha-tocopherol every other day) in healthy men (actually healthy physicians-an oxymoron?), both supplements were found to have no impact on prostate cancer (no increase or decrease in risk)! And, even though the trial ended in 2007, many participants were still followed to determine the more long-term impact of these supplements and again nothing was found.¹ In other words, perhaps we are worrying too much about vitamin E and prostate cancer. But there is still no reason to buy or use these supplements if you have prostate cancer or are trying to prevent prostate cancer (the amount in most single pill per day multivitamins are not a concern).

Okay, the 2014 World Cup Final is over, which means I no longer walk around my house anymore yelling "GOALLLLLLLLLLLLLLL!!!" because my wife, kids and dog will be completely annoyed, as they were during the tournament. But at least I had an excuse why it was necessary during this time. Now, on to what is new in the prostate cancer front and supplements and the answer is NOTHING! Nada! Zilch! Now, this is not a bad thing but may actually be a good thing! Why? I am glad I asked myself this question. Over the past several years I and many others have warned folks that vitamin E supplements can increase the risk of prostate cancer because of findings from the notable SELECT trial. However, what got missed in all the cacophony is the actual or absolute risk of getting prostate cancer from vitamin E supplements. While higher than average, overall, it is only minimally increased. And, results from another large U.S. trial (PHS2) has now suggested that there is neither an increased or decreased risk of prostate cancer due to intake of vitamin E or vitamin C supplements. In fact, in the latest update from this U.S. trial, again

known as PHS2, researchers found nothing except a suggestion that vitamin C (not vitamin E) supplements might significantly lower colorectal cancer risk in men! Hey, why didn't this receive more attention?

So, what are you supposed to do with all this information? Basically, nothing has changed and I do not believe anyone diagnosed or treated for prostate cancer should take an individual vitamin E supplement. And, if you want to take a vitamin C supplement to prevent colds or because you think it is immune healthy, then go ahead and take it. But keep in mind that vitamin C can increase your risk of developing a kidney stone. I take vitamin C supplements when I train for marathons or half-marathons as a means to reduce my risk of catching colds (which is where most of the positive research is for vitamin C), so it keeps me healthy enough to wait in the dark in my house and when my wife and kids come home from the store I turn on the lights and yell "GOALLLLLLLLLLLLLLL!!!"

Reference:

1. Wang L, Sesso HD, Glynn RJ, et al. Vitamin E and C supplementation and risk of cancer in men: posttrial follow-up in the Physicians' Health Study II randomized trial. *Am J Clin Nutr* 14 July 2014, Epub.



SERUM ALKALINE PHOSPHATASE DIFFERENTIATES PROSTATE-SPECIFIC ANTIGEN FLARE FROM EARLY DISEASE PROGRESSION AFTER DOCETAXEL CHEMOTHERAPY IN CASTRATION-RESISTANT PROSTATE CANCER WITH BONE METASTASIS

Han KS, Hong SJ

J Cancer Res Clin Oncol
4 May 2014; Epub

Purpose: A transient rise in prostate-specific antigen (PSA) after the initiation of chemotherapy, known as PSA flare, has been frequently reported in patients with castration-resistant prostate cancer (CRPC). But there has been no way to differentiate PSA rises in CRPC. We investigated whether bone-related serum markers differentiate PSA flare from progression in CRPC patients with bone metastasis.

Methods: We reviewed CRPC patients with bone metastasis who received systemic chemotherapy from 2002 to 2008. Pretreatment baseline and follow-up data including age, performance score, PSA, Gleason score, alkaline phosphatase (ALP), calcium level, and hemoglobin were evaluated. Pretreatment parameters and follow-up serum parameters after the first cycle of chemotherapy were included in statistical analyses.

Results: PSA increased in 38 patients (45.8 %) at the first evaluation after chemotherapy. Among the PSA rises, PSA increased continuously or did not decrease to the stabilization level by the third evaluation in 22 (26.5 %) patients, while PSA decreased to the stabilization or response level by the third evaluation in 16 (19.3 %). PSA flare occurred in 17 (20.5 %). The univariate analyses showed that no baseline parameters were associated with PSA flare, but the initial ALP decrease, changed ALP ratio, and median calcium level were significantly associated with PSA flare ($p = 0.001$, $p = 0.008$ and $p = 0.012$, respectively). Multivariate logistic regression analysis showed that a change in the ALP level is an independent predictive factor for PSA flare ($p = 0.017$).

Conclusions: ALP is a useful biomarker to differentiate PSA flare from early PSA progression during docetaxel chemotherapy in CRPC patients with bone metastasis.

GETTING BACK TO EQUAL: THE INFLUENCE OF INSURANCE STATUS ON RACIAL DISPARITIES IN THE TREATMENT OF AFRICAN AMERICAN MEN WITH HIGH-RISK PROSTATE CANCER

Mahal BA, Ziehr DR, Aizer AA, et al
Urol Oncol 17 May 2014; Epub

Objectives: Treating high-risk prostate cancer with definitive therapy improves survival. We evaluated whether having health insurance reduces racial disparities in the use of definitive therapy for high-risk prostate cancer.

Materials and Methods: The Surveillance, Epidemiology, and End Results Program was used to identify 70,006 men with localized high-risk prostate cancer (prostate-specific antigen level $>20\text{ng/ml}$ or Gleason score 8-10 or stage $>cT3a$) diagnosed from 2007 to 2010. We used multivariable logistic regression to analyze the 64,277 patients with complete data to determine the factors associated with receipt of definitive therapy.

Results: Compared with white men, African American (AA) men were significantly less likely to receive definitive treatment (adjusted odds ratio [AOR] = 0.60; 95% CI: 0.56-0.64; $P < 0.001$) after adjusting for sociodemographics and known prostate cancer prognostic factors. There was a significant interaction between race and insurance status ($P_{\text{interaction}} = 0.01$) such that insurance coverage was associated with a reduction in racial disparity between AA and white patients regarding receipt of definitive therapy. Specifically, the AOR for definitive treatment for AA vs. white was 0.38 (95% CI: 0.27-0.54, $P < 0.001$) among uninsured men, whereas the AOR was 0.62 (95% CI: 0.57-0.66, $P < 0.001$) among insured men.

Conclusions: AA men with high-risk prostate cancer were significantly less likely to receive potentially life-saving definitive treatment when compared with white men. Having health insurance was associated with a reduction in this racial treatment disparity, suggesting that expansion of health insurance coverage may help reduce racial disparities in the management of men with aggressive cancers.

18F-DCFCB AND PET/CT

(Continued from page 1)

was 58.0 ng/mL. Rising PSA levels and radiographic evidence on conventional imaging (CT or bone scan) indicated new or progressive prostate cancer. Five of the patients had castration-sensitive disease and seven had CRPC.

Two hours after the men were injected with approximately 10 mCi of 18F-DCFCB, PET/CT images were used to measure the maximum standardized uptake value (SUV_{max}) of the tracer.

“We didn’t see any significant difference in the level of uptake between hormone-sensitive and hormone-resistant disease,” Dr. Rowe reported (average SUV_{max} , 10.6 vs. 11.6; $P = 0.41$).

“However, with higher levels of uptake in the bone lesions of men with resistant disease, there was a trend toward significance,” he added (average SUV_{max} 11.7 vs. 5.1; $P = 0.049$).

“The arrival of 18F-DCFCB and the finding that it is still useful in CRPC should hasten the development of PSMA-directed therapies,” noted Peter Choyke MD, senior investigator for the Molecular Imaging Program at the National Cancer Institutes, in an email to Medscape Medical News.

The new tracer “will be especially useful in restaging patients after the biochemical recurrence of prostate cancer and in monitoring patients with more advanced disease,” he added.

Presented at the 2014 SNMMI Annual meeting, Abstract 19, 8 June 2014

Medscape Medical News, 10 June 2014



VASECTOMY AND PROSTATE CANCER – HOW SERIOUS IS THE LINK?

Men who had a vasectomy had a significantly greater risk of developing aggressive, potentially fatal prostate cancer, according to data from a 50,000-patient cohort study.

Overall, vasectomy increased the risk of prostate cancer by about 10%, increasing to about 20% for high-grade and lethal cancers. A subgroup analysis showed more than a 50% greater risk of prostate cancer among men who underwent regular prostate-specific antigen (PSA) screening for prostate cancer, as reported online in the *Journal of Clinical Oncology*.

The authors emphasized that the overall association between vasectomy and prostate cancer was modest.

“The cumulative incidence of lethal prostate cancer during a 24-year follow-up was 1.6%,” Lorelei A. Mucci, ScD, of Harvard School of Public Health, and colleagues concluded. “Thus, these relative risks translate into small increases in absolute risk. The decision to opt for a vasectomy remains a highly personal one in which the potential risks and benefits must be considered.”

A urologist who has studied lifestyle factors associated with prostate cancer said the results reinforce a previously reported link between vasectomy and prostate cancer, but seconded the notion that the association is modest.

“I think we need to tell men that vasectomy has some risk with prostate cancer, may be linked, but we don’t know,” said Stephen Freedland, MD, of Duke University. “It’s something they need to be aware of and monitored, but really, to me, this is not something that is such a strong association that we need to be changing the way we practice, either prostate cancer screening or vasectomy.”

Cohort and observational studies dating back to the early 1990s have yielded conflicting results about the association between vasectomy and prostate cancer.

Some studies have shown as much as a twofold increase in the risk of prostate cancer after vasectomy, whereas others showed no association, the authors noted.

Studies showing positive associations have been criticized for potential detection bias and confounding by several factors. To address the shortcomings of previous investigations, Mucci and colleagues examined the association between vasectomy and prostate cancer among participants in the Health Professionals Follow-Up Study, which involved men who were ages 40 to 75 at enrollment in 1986.

During follow-up through 2010, 6,023 participants had newly diagnosed prostate cancer, including 811 lethal cases. The data showed that 12,321 of the men had vasectomies. The primary outcomes were the relative risk (RR) of total, advanced, high-grade, and lethal prostate cancer, adjusted for a variety of possible confounders.

The results showed association between vasectomy and an increased risk of:

- Total prostate cancer: RR 1.10, 95% CI 1.04-1.17
- High-grade disease (Gleason score 8-10): RR 1.22, 95% CI 1.03-1.45
- Lethal prostate cancer (death or distant metastases): RR 1.19, 95% CI 1.00-1.43

The authors identified a stronger association between vasectomy and prostate cancer among men who had regular screening PSA tests for prostate cancer (RR 1.56, 95% CI 1.03-2.36).

Vasectomy did not have a significant association with low-grade or localized prostate cancer.

“Additional analyses suggested that the associations were not driven by differences in sex hormone levels, sexually transmitted infections, or cancer treatment,” the authors said of their findings.

“The study adds information to the discussion and controversy surrounding vasectomy and prostate cancer but leaves many questions unanswered,” said Gerald Andriole, MD, of Washington University in St. Louis, MO.

“What limits the robustness of the finding is that there are potentially many unknown confounders that could explain the excess cancer and high-grade disease in men who had vasectomy,” Andriole told MedPage Today by email. “For example, did men in each group

seek equivalent treatments for benign prostatic hyperplasia? If so, did they receive 5-alpha reductase inhibitors, which may affect the number of men undergoing biopsy of the prostate and the Gleason score of the cancer, in equal frequency.

“Use of transurethral resection of the prostate, statins, selenium, and a number of other factors can influence prostate cancer risk,” he added.

“The study added little information that goes beyond what previous studies had shown,” said Gregory Zagaja, MD, of the University of Chicago. “The study suffered from the same limitations of studies that came before it.

“These population-based studies are significantly flawed in that there is no mention as to the incidence of prostate cancer screening in the study population,” Zagaja said in an email. “If the incidence of screening was different between the vasectomy cohort when compared to the nonvasectomy group, this can significantly account for the differences seen in the study. This would also influence the differences seen in high-risk and lethal prostate cancer.”

Freedland, Andriole, and Zagaja all said that no consensus exists about potential biological explanations for reported associations between vasectomy and prostate cancer or whether the association is biologically plausible.

“The fact that the same type of specialist – a urologist – performs vasectomies and diagnoses prostate cancer is another issue,” Freedland said.

“If you have a vasectomy and you’re at higher risk, is it because you have a higher risk of developing prostate cancer or is it because you’re seeing the doctor who diagnoses your cancer, so you’re going to be screened more closely?” he said.

MedPage Today, 9 July 2014



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COMBINING PROSTATE-SPECIFIC ANTIGEN NADIR AND TIME TO NADIR ALLOWS FOR EARLY IDENTIFICATION OF PATIENTS AT HIGHEST RISK FOR DEVELOPMENT OF METASTASIS AND DEATH FOLLOWING SALVAGE RADIATION THERAPY

Jackson W, Johnson S, Foster B, et al
Pract Radiat Oncol 4(2):99-107, 2014

Purpose: Little is known regarding the prognostic capability of prostate-specific antigen (PSA) nadir (nPSA) and time to nPSA (TnPSA) following salvage radiation therapy (SRT) for biochemical failure (BF) post radical prostatectomy (RP). We sought to assess their prognostic significance in this setting.

Methods and materials: A total of 448 patients who received SRT without androgen deprivation therapy at a single academic institution were included in this retrospective analysis. Univariate analysis and multivariate Cox proportional hazards models were used to assess BF, distant metastasis (DM), prostate cancer-specific death (PCSD), and overall survival (OS). A prognostic nomogram incorporating nPSA and TnPSA was developed and validated in randomly allocated training and validation cohorts.

Results: Median follow-up post-SRT was 64 months. Median nPSA and TnPSA were undetectable and 6.7 months, respectively. On univariate analysis, a detectable nPSA ($p < 0.01$) and TnPSA < 6 months ($p < 0.01$) were predictive of all outcomes. In a training cohort, a 14-point nomogram incorporating detectable nPSA, TnPSA, Gleason score, pre-radiation therapy PSA, and seminal vesicle invasion predicted BF (hazard ratio [HR], 1.4; $p < 0.0001$), DM (HR, 1.3; $p < 0.0001$), PCSD (HR, 1.3; $p < 0.0001$), and decreased OS (HR, 1.2; $p < 0.0001$). Adding nPSA and TnPSA improved the prognostic value of the nomogram compared to using clinical predictors only. The nomogram was evaluated in a validation cohort where it was predictive of BF (c-index = 0.77), DM (0.73), and PCSD (0.69).

Conclusions: Patients with a detectable nPSA also having a TnPSA < 6 months post-SRT are at high-risk for DM, PCSD, and decreased OS. These patients are unlikely to have clinically localized disease and should be considered for initiation of systemic therapies.

INTOLERANCE OF UNCERTAINTY, COGNITIVE COMPLAINTS, AND CANCER-RELATED DISTRESS IN PROSTATE CANCER SURVIVORS

Eisenberg S, Kurita K, Taylor-Ford M, et al
Psychooncology 2 June 2014; Epub

Objective: Prostate cancer survivors have reported cognitive complaints following treatment, and these difficulties may be associated with survivors' ongoing cancer-related distress.

Intolerance of uncertainty may exacerbate this hypothesized relationship by predisposing individuals to approach uncertain situations such as cancer survivorship in an inflexible and negative manner. We investigated whether greater cognitive complaints and higher intolerance of uncertainty would interact in their relation to more cancer-related distress symptoms.

Methods: This cross-sectional, questionnaire-based study included 67 prostate cancer survivors who were three to five years post treatment. Hierarchical multiple regression analyses tested the extent to which intolerance of uncertainty, cognitive complaints, and their interaction were associated with cancer-related distress (measured with the Impact of Event Scale-Revised; IES-R) after adjusting for age, education, physical symptoms, and fear of cancer recurrence.

Results: Intolerance of uncertainty was positively associated with the IES-R avoidance and hyperarousal subscales. More cognitive complaints were associated with higher scores on the IES-R hyperarousal subscale. The interaction of intolerance of uncertainty and cognitive complaints was significantly associated with IES-R intrusion, such that greater cognitive complaints were associated with greater intrusive thoughts in survivors high in intolerance of uncertainty but not those low in it.

Conclusions: Prostate cancer survivors who report cognitive difficulties or who find uncertainty uncomfortable and unacceptable may be at greater risk for cancer-related distress, even three to five years after completing treatment. It may be beneficial to address both cognitive complaints and intolerance of uncertainty in psychosocial interventions.

NEW ANDROGEN RECEPTOR INHIBITOR SHOWS ACTIVITY IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER

ODM-201 is a novel androgen receptor inhibitor, structurally distinct from enzalutamide, that acts via high-affinity binding to the androgen receptor and inhibition of receptor nuclear translocation. In the phase I/II ARADES trial reported in *The Lancet Oncology*, Fizazi et al identified no maximum tolerated dose and observed PSA responses in men with progressive metastatic castration-resistant prostate cancer (CRPC).

In this study, conducted in 23 U.S. and European hospitals, no dose-limiting toxicity or maximum tolerated dose was found at an oral ODM-201 dose range of 200 mg to 1,800 mg daily in the phase I portion. In the phase II portion, 110 men were randomly assigned to receive doses of 200 mg ($n = 38$), 400 mg ($n = 37$), or 1,400 mg ($n = 35$); four, seven, and three men treated at these dose levels in the phase I portion were also advanced to phase II evaluation. The primary endpoint was $\geq 50\%$ reduction in serum PSA at week 12.

Among evaluable men, PSA response at 12 weeks was observed in 29, 33, and 33% at 200, 400 mg, and 1,400 mg/day, respectively. Response rates were higher among men who were chemotherapy-naïve and had not received CYP17 inhibitor treatment. Follow-up is ongoing.

No dose-related trends in adverse events were observed. The most common adverse events of any grade in all patients in the phase II study were fatigue/asthenia (34%), back pain (25%), and arthralgia (21%). The most common grade 3 adverse events were fatigue/asthenia, back pain, arthralgia, pain, and anemia, all of which occurred in 2% of men. Grade 4 adverse events occurred in two patients (2%). Treatment was discontinued due to adverse events in 3%, with none of these adverse events being considered related to ODM-201 treatment.

The investigators concluded, "Our results suggest that ODM-201 monotherapy in men with progressive metastatic castration-resistant prostate cancer provides disease suppression and that ODM-201 has a favourable safety profile. These findings support further investigation of clinical responses with ODM-201 in men with castration-resistant prostate cancer."

The ASCO Post, 15 July 2014

CIRCUMCISION MAY CUT RISK OF PROSTATE CANCER

Greatest protective effect observed in men circumcised at age 36+ years old

Circumcision appears to confer a protective effect against the development of prostate cancer (PCa), especially among those circumcised at age 36 years or older and black men, according to research published online ahead of print in *BJU International*.

Andrea R. Spence, PhD, of the University of Quebec in Laval, Canada, and colleagues conducted a case-control study involving 1,590 prostate cancer cases and 1,618 age-matched population controls. Overall, compared with uncircumcised men, circumcised men had a non-significant 11% decreased risk of PCa. Men circumcised at age 36 years or older had a significant 45% decreased risk of PCa.

The protective effect of circumcision against PCa was weaker among men who were circumcised within one year of birth. Among black men, a group that has the highest rate of PCa, circumcision was associated with a significant 60% decreased risk of PCa. No association between circumcision and PCa risk was among other ancestral groups.

Renal & Urology News, July 2014

GAY MEN & PROSTATE CANCER

(Continued from page 1)

Results: Compared with norms, GMP-Ca reported significantly worse functioning and more severe bother scores on urinary, bowel, hormonal symptom scales ($P < 0.015-0.0001$), worse mental health functioning ($P < 0.0001$), greater fear of cancer recurrence ($P < 0.0001$), and were more dissatisfied with their PCa medical care. However, GMP-Ca reported better sexual functioning scores ($P < 0.002$) compared with norms. Many of the observed differences met criteria for clinical significance. Physical functioning HRQOL and sexual bother scores were similar to that of published samples. GMPCa tended to be more "out" about their sexual orientation than other samples of gay men.

Conclusions: GMPCa reported substantial changes in sexual functioning after PCa treatment. They also reported significantly worse disease-specific and general HRQOL, fear of recurrence, and were less satisfied with their medical care than other published PCa samples. Sexual health providers must have an awareness of the unique functional and HRQOL differences between gay and heterosexual men with PCa.



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