Us TOO® PROSTATE CANCER EDUCATION & SUPPORT

HOTSHEET

FEBRUARY 2012

OUTERCOURSE VS. INTERCOURSE REVISITED

By Dr. Jo-an Baldwin Peters

The second "Outercourse vs. Intercourse," follow-up online survey was a joint, unfunded, effort by Dr. Jo-an Baldwin Peters (PhD), Court Brooker a prostate cancer survivor and communications expert, as well as Dr. Joel Funk, Assistant Professor of Surgery, University of Arizona Tucson. It was designed and compiled by Dr. Jo-an Baldwin Peters and Court Brooker.

The online survey commenced on 19 October 2009 and ended on 29 October 2010. There were 651 respondents comprising of 448 prostate cancer survivors and 203 partners. It was disappointing that so few partners took the opportunity to voice their opinions and provide input towards solutions.

The prostate cancer patients responding to the survey came from the US (78%), Canada (19%), Australia (2%), United Kingdom (1%) and Venezuela, France, Greece, Holland, Hungary, Israel, Japan, Mongolia, Spain, South Africa and Switzerland (all <1%).

The men ranged in age from 42 to 84 and the partners from 36 to 80.

Fifty percent of the men had prostatectomies of which 14% were performed by Robotic surgery. Twenty-one percent

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STATINS TIED TO LOWER RISK OF FATAL PROSTATE CANCER

In a new study of middle-aged New Jersey men, statin therapy was linked to a lower risk of death from prostate cancer. Most of the men were white and in their mid- to late-60s, on average. Close to 25% had ever taken a statin. The researchers found that men who died of prostate cancer were half as likely to have taken a statin at any time, and for any duration, than men in the control group.

"People may be on these medications for their heart, but it may actually be doing them some good for their prostate," study author Dr. Stephen Marcella, from the University of Medicine and Dentistry of New Jersey in New Brunswick, told Reuters Health.

Dr. Marcella and his colleagues collected the medical records of 380 men who had died of prostate cancer and another 380 age- and race-matched controls. After adjustment for weight, comorbidities, and medications, men with fatal prostate cancer were 63% less likely to have ever taken a statin, according to findings published online December 16 in the journal *Cancer*.

But, Dr. Marcella added, "I would not tell a person if they don't have a risk of heart disease, (if) they don't have hypertension... to take a statin just to prevent lethal prostate cancer." And even if

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'AMAZING' PROSTATE CANCER MARKER PAPER NOW RETRACTED

A cloud has descended over research into a biomarker for prostate cancer – early prostate cancer antigen-2 (EPCA-2) – which was described as "amazing" and appeared to overcome some of the shortcomings of prostate-specific antigen.

A paper about EPCA-2 was published in 2007 in *Urology*, but was retracted in October 2011 because data from the study could not be verified. "The article contains findings that may be unreliable," the study authors write in their retraction, which was highlighted in the Retraction Watch blog <http:/ retractionwatch.wordpress.com/2012/01/04/hopkins-scientists-retract-prostate-cancer-screening-study-at-center-of-2009-lawsuits/>.

The paper's lead author is Robert H. Getzenberg, PhD, director of research of the James Buchanan Brady Urological Institute and professor of urology at the Johns Hopkins University School of Medicine in Baltimore, Maryland.

Dr. Getzenberg holds a patent for the assay technology that detects EPCA-2. The patent is owned by the University of Pittsburgh and Johns Hopkins University and has been licensed to Onconome Inc. Dr. Getzenberg received research funding from Onconome, which, in 2009, sued him and the 2 institutions for scientific fraud.

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MAGNETIC RESONANCE IMAGING GUIDED PROSTATE BIOPSY IN MEN WITH REPEAT NEGATIVE BIOPSIES AND INCREASED PROSTATE SPECIFIC ANTIGEN

Hambrock T, Somford DM, Hoeks C, et al

J Urol 183: 520-8, 2010

Purpose: Undetected cancer in repeat transrectal ultrasound (TRUS) guided prostate biopsies in patients with increased prostate specific antigen (PSA) >4 ng/mL is a considerable concern. We investigated the tumor detection rate of tumor suspicious regions on multimodal 3 Tesla magnetic resonance imaging (MRI) and subsequent MRI guided biopsy in 68 men with repeat negative TRUS guided prostate biopsies. We compared results to those in a matched TRUS guided prostate biopsy population. Also, we determined the clinical significance of detected tumors.

Materials and Methods: A total of 71 consecutive patients with PSA >4 ng/mL and 2 or greater negative TRUS guided prostate biopsy sessions underwent multimodal 3 Tesla MRI. In 68 patients this was followed by MRI guided biopsy directed toward tumor suspicious regions. A matched multisession TRUS guided prostate biopsy population from our institutional database was used for comparison. The clinical significance of detected tumors was established using accepted criteria, including PSA, Gleason grade, stage and tumor volume.

Results: The tumor detection rate of multimodal 3 Tesla MRI guided biopsy was 59% (40 of 68 cases) using a median of 4 cores. The tumor detection rate was significantly higher than that of TRUS guided prostate biopsy in all patient subgroups ($p < 0.01$) except in those with PSA >20 ng/mL, prostate volume greater than 65 cc and PSA density greater than 0.5 ng/mL/cc, in which similar rates were achieved. Of the 40 patients with identified tumors 37 (93%) were considered highly likely to harbor clinically significant disease.

Conclusions: Multimodal MRI is an effective technique to localize prostate cancer. MRI guided biopsy of tumor suspicious regions is an accurate method to detect clinically significant prostate cancer in men with repeat negative biopsies and increased PSA.

DOCETAXEL-BASED THERAPY WITH OR WITHOUT ESTRAMUSTINE AS FIRST-LINE CHEMOTHERAPY FOR CASTRATION-RESISTANT PROSTATE CANCER: A META-ANALYSIS OF FOUR RANDOMIZED CONTROLLED TRIALS

Qi WX, Shen Z, Yao Y

J Cancer Res Clin Oncol 137: 1785-90, 2011

Purpose: To assess the efficacy and toxicity of the addition of estramustine to docetaxel-based chemotherapy for the treatment of castration-resistant prostate cancer (CRPC).

Methods: We systematically searched, without language restrictions, for randomized clinical trials that compared docetaxel-based chemotherapy with or without estramustine in patients with histologically proven prostate cancer. The primary end point was overall survival (OS). Secondary endpoints were prostate-specific antigen (PSA) response rate and grade 3 or 4 toxicity. Data was extracted from the studies by two independent reviewers. The meta-analysis was performed by Stata version 10.0 software (College Station, Texas, USA).

Results: Four randomized clinical trials (totally 400 patients) were eligible. Meta-analysis showed that there was significant improvement in PSA response rate in docetaxel-based therapy with estramustine group, compared with docetaxel-based therapy group (OR = 1.55, 95% CI = 1.10-2.18, P = 0.012). With regard to OS (HR = 0.873, 95% CI = 0.55-1.40, P = 0.572), grade 3 or 4 neutropenia (OR = 1.27, 95% CI = 0.61-2.7), anemia (OR = 1.04, 95% CI = 0.07-16.3), thrombocytopenia (OR = 0.87, 95% CI = 0.13-5.7), diarrhea (OR = 2.3, 95% CI = 0.36-14.9), nausea (OR = 1.14, 95% CI = 0.16-8.35), mucositis (OR = 1.66, 95% CI = 0.50-5.52) , and vomiting (OR = 1.53, 95% CI = 0.23-10.3), and there were no significant differences between the two groups.

Conclusions: This was the first meta-analysis of docetaxel-based therapy with estramustine versus docetaxel-based chemotherapy in the treatment of CRPC. Our meta-analysis did not support the addition of estramustine to docetaxel-based chemotherapy for the treatment of CRPC, based on no gain in survival.

ASK DOCTOR SNUFFY MYERS

Editors' note: *This column contains opinions and thoughts of its author and are not necessarily those of Us TOO International.*

I have just been diagnosed with prostate cancer. My PSA is 4.2 ng/ml and the Gleason was 3+3=6. The cancer was 5% of one core. I am age 52. My urologist recommends radical prostatectomy, but I newly married and my wife, age 38, is interested in starting a family. Do I need surgery? Even with surgery, I have a cancer and we are worried I might not live long enough to raise the children. What would you advise?

First, a small Gleason 6 prostate cancer is very unlikely to kill you no matter what treatment option you select. In fact, you are much more likely to die of something else. So, your first step should be to have a complete health inventory to rule out cardiovascular disease and colon cancer. I presume you are smart enough not to smoke or are motivated to stop.

Now that we have the basics out of the way, how dangerous is your cancer? I would note that this small Gleason 6 cancer can be found in 30-50%of men your age group. Only a small percentage of these cancers has the capacity to grow and spread. There is now a broad consensus that you could do active surveillance. This is an approach where you are followed carefully and sent to surgery or radiation if your cancer is growing. While we have used color Doppler ultrasound to follow Gleason 6 cancers, MRI also appears to be quite useful. It appears that any Gleason 6 likely to cause a problem will show changes on MRI before it poses any risk of spread.

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US TOO WANTS TO ANSWER YOUR QUESTIONS!

Dr. Myers would love to provide direct answers to questions posed by Us TOO members. Instead of printing questions answered in the *Prostate Forum*, we'd rather provide readers who subscribe to both publications with fresh content. Questions about imaging, active surveillance, and biochemical relapse would be particularly appreciated right now.

Send questions to <Jackie@ustoo.org> or call the Helpline at 800-808-7866.

PROTON THERAPY EFFECTIVE PROSTATE CANCER TREATMENT

Proton therapy, a type of external beam radiation therapy (EBRT), is a safe and effective treatment for prostate cancer, according to two new studies published in the January issue of the International Journal of Radiation Oncology• Biology •Physics (Red Journal), the American Society for Radiation Oncology's (ASTRO) official scientific journal.

In the first study, researchers at the University of Florida in Jacksonville, Fla., prospectively studied 211 men with low-, intermediate-, and high-risk prostate cancer. The men were treated with proton therapy, a specialized type of EBRT that uses protons instead of X-rays. After a two year follow-up, the research team led by Nancy Mendenhall, MD, of the University of Florida Proton Therapy Institute, reported the treatment effective and that the gastrointestinal and genitourinary side effects were generally minimal.

In the second study, researchers from Massachusetts General Hospital in Boston, MA, Loma Linda University Medical Center in Loma Linda, CA, and the Radiation Therapy Oncology Group in Philadelphia performed a case-matched analysis comparing high-dose EBRT using a combination of photons (X-rays) and protons with brachytherapy (BT) e.g., radioactive seed implants.

Over three years, 196 patients received EBRT. Their data was compared to 203 men of similar stages who received BT over the same time period. Researchers then compared the biochemical failure rates (a statistical measure of whether the cancer relapses) and determined that men who received the proton/photon therapy had the same rate of recurrence as the men who received BT.

"For men with prostate cancer, BT and EBRT using photons and protons are both highly effective treatments with similar relapse rates," John J. Coen, MD, a radiation oncologist at Massachusetts General Hospital in Boston, said. "Based on this data, it is our belief that men with prostate cancer can reasonably choose either treatment for localized prostate cancer based on their own concerns about quality of life without fearing they are compromising their chance for a cure."

ASTRO news release, 5 January 2012

EPCA-2 PAPER RETRACTED

(Continued from page 1)

Dr. Getzenberg at one time reportedly described EPCA-2 as "amazing" because of its very high sensitivity and specificity, according to Retraction Watch. A critic of EPCA-2 said that he has attempted for some time to publish a letter in *Urology* on the shortcomings of the assay used by Dr. Getzenberg and colleagues in their EPCA-2 research.

"This letter was accepted for publication, but has never been published and the reasons for the delay not resolved," said Eleftherios Diamandis, PhD, from the Department of Laboratory Medicine and Pathobiology at the University of Toronto in Ontario, Canada, in an essay published in Clinical Chemistry last year.

Dr. Diamandis said that he knew that the assay used to detect EPCA-2 was not capable of its touted abilities "as soon as the first paper on EPCA-2 was published. By analyzing what we know about ELISA assay design and performance, I concluded that the assay would not be either a sensitive or a specific measure of any analyte present in serum at the low ng/mL concentrations," he writes.

When his letter languished at *Urology*, he turned to the journal *Clinical Chemistry* to publish his insights. In his essay, Dr. Diamandis frames the EPCA-2 debacle in a larger cultural context: few biomarkers are validated but many are touted as the next great thing.

"The literature is full of reports of high-profile papers that have reported excellent diagnostic discrimination between groups, but subsequent independent validation was a failure," he writes. In most cases, various biases were critical factors, he says. One example is the nuclear magnetic resonance profiling of urine for cancer detection, which has failed repeated validation efforts.

Dr. Diamandis has commented on this issue in other papers. Last year in the *Journal of the National Cancer Institute*, he stated that not a single new "major cancer biomarker" has been approved for clinical use in the past 2 decades, despite large amounts of funding and plenty of public-relations hype, as reported then by Medscape Medical News.

Medscape Medical News, 5 January 2012

OUTERCOURSE VS. INTERCOURSE SURVEY *(Continued from page 1)*

had radiation, 16% hormone deprivation 7% brachytherapy (radioactive seed implants), and 2% had chemotherapy, cryotherapy and active surveillance. Less than 1% received HIFU.

Prior to prostate cancer treatment:

- Five percent of the survivors were sexually inactive and this rose to 52% post treatment
- Four percent of the partners were sexually inactive and this rose to 46% post treatment.
- Forty-four percent of the survivors and partners had sex once to twice a week and post treatment 11% and 8%
- Eleven percent of the survivors had sex three times or more per week and remained the same post treatment.
- Eighteen percent of the partners had sex three times a week or more and 8% post treatment

When asked "how important it is to experience an orgasm on a regular basis even if it did not result from penetrative sex," 60% of the men felt it was important or very important as did 49% of the partners. Only 8% of the survivors and partners felt it was not important.

Ninety-four percent of the survivors and 86% of the partners answered the question on "What forms of assistance resulted in orgasm with or without penetration?" There was concurrence between survivors and partners on the success rate for various types of assistance with one exception namely penile shots.

- Penile shots – survivors 71% and partners 43%
- Self-masturbation 76%
- Mutual masturbation 70%
- Penile implants 67% (small sample)
- Oral sex 61%
- Sex toys (vibrators, books, CDs) – survivors 56% and partners 64%
- Oral medication 52%
- Pump 43%
- Urethral suppositories 33%

The survey protagonists recognize the importance of maintaining sexuality. In order to do this, honest communication skills between partners needs improvement and constant work.

The identity of the participants was protected and every effort has been taken to ensure this. Our data analysis, to date, is basic. We neither have the finances or current expertise to develop it further.

We'd be happy for interested researcher to assist us.

To review all survey questions, respondent demographics and graphs of answers, visit www.pcainaz.org/survey.

For a follow-up article on maintaining sexuality titled "Erectile Dysfunction! Disown It Or Own it!" and more resources, visit www.pcainaz.org/articles.

For her original article on the Us TOO website, go to: http://www.ustoo.org/Support_Companion_Family.asp.

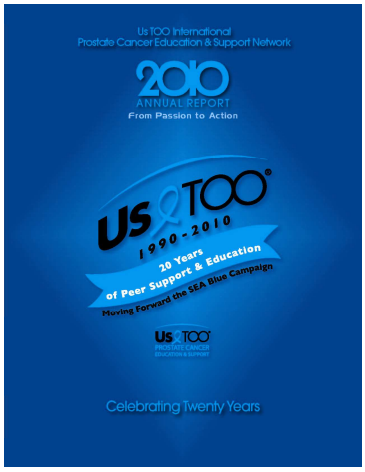
Dr. Jo-an Baldwin Peters *is the wife of a prostate cancer survivor. A trained physical therapist, she also has an MSc in Biostatistics and Epidemiology and a PhD in Health Care Administration.*

Dr. Peters' recent research has focused on the effects of prostate cancer treatment on couples' sexual experiences and this became her dissertation. She published her findings in an article for Us TOO "Outercourse vs. Intercourse," one of the most frequently downloaded files on the Us TOO website. The recent online sexuality survey is an extension of her dissertation and is the basis for this update of her original research.

NEW ON WWW.USTOO.ORG

Recent additions to the Us TOO website include:

See new online map of all Us TOO support group locations @ www.ustoo.org/map



Read the just-published Us TOO Annual Report for 2010

And MORE!

- Meet the new Us TOO International Chairman & Board of Directors
- A look back on 2011:

  Recognizing Business Leadership Council members and supporters,

  Edward C. Kaps Hope Award Recipients &

  Us TOO fundraisers

Questions and concerns about prostate cancer? Talk to others online in the Us TOO Inspire Prostate Cancer Discussion Community @ *ustoo.inspire.com*

Help spread the word about Us TOO: Become a FAN on Facebook!

ROBOT PROSTATECTOMY NO LESS LIKELY TO LEAVE PATIENTS DISAPPOINTED

In a recent survey, men who had robotic surgery for prostate cancer and men who had lower-tech surgeries were equally likely to have sexual problems and urinary leakage afterward.

The new study, published online January 3rd in the *Journal of Clinical Oncology*, is based on responses from more than 600 prostate cancer patients on Medicare, including roughly 400 who had robotic-assisted laparoscopic prostatectomy (RALP). Nearly 90% had a moderate or major problem with sexual functioning 14 months after their surgery, Dr. Michael Barry of Massachusetts General Hospital in Boston and colleagues found. And about 33% reported incontinence afterward. Overall, there were no differences between the two patient groups, although urinary problems appeared to be slightly more common after the RALP procedure.

An editorial in the journal called the findings "sobering," but added that it's hard to compare the two procedures directly based on the survey results. It's possible, for instance, that men with high hopes for RALP would be particularly bothered by side effects afterward.

"The problem that is revealed in this paper is this question of expectations," said Dr. Matthew Cooperberg, a urologist at the University of California, San Francisco who co-wrote the editorial. Out of the tens of thousands prostate removals done annually in the US, some 85 percent are estimated to be RALP.

"To an extent it's the manufacturer, to an extent it's surgeons, to an extent it's a culture that tends to put great faith in technology, even when the patient doesn't understand it," said Cooperberg.

The robots, which cost a couple of million dollars each, do have some advantages, such as less blood loss. But Cooperberg, who uses the technology himself, readily acknowledges that it probably doesn't treat cancer any better than the old surgery and doesn't have proven benefit in terms of side effects.

Reuters Health, 9 January 2012

HORMONAL PROSTATE CANCER THERAPY TIED TO BLOOD CLOTS

Hormone-targeted therapy for prostate cancer may raise the risk of potentially dangerous blood clots, a large US study suggests. Analyzing data on more than 154,000 older men with prostate cancer, researchers found that those who received hormonal therapy (HT) had double the rate of blood clots in the veins, arteries or lungs compared to men not on the treatment. Men who developed blood clots ended up in the hospital about one-quarter of the time, the researchers report online in the journal *Cancer* on 9 November 2011.

Of the 58,000-plus men taking HT, 15 percent developed a blood clot over roughly four years, versus seven percent of men who did not receive get HT.

"By no means is this a trivial risk," said lead author Dr. Behfar Ehdaie, of Memorial-Sloan Kettering Cancer Center in New York. For men weighing their options for prostate cancer treatment, Ehdaie said the risk of blood clots – and other side effects – needs to be balanced against the benefits. Other HT side effects can include weight gain, bone thinning, hot flashes and erectile dysfunction.

The approach is based on the fact that testosterone can fuel the growth of prostate cancer. Curbing a man's production of the hormone – by surgical removal of the testicles or, far more often, medication – can be helpful.

As for why HT would promote blood clots, the mechanisms are uncertain. In fact, the current findings do not prove that the therapy itself is the direct cause of men's blood clots. Ehdaie's team tried to account for other factors that could explain the link; and they did find that men on HT tended to be older and in poorer overall health.

But even with those differences considered, men on HT had a 56 percent greater chance of developing a blood clot. And the clot risk generally climbed the longer a man was on the treatment.

"We can't infer causality, but it is a strong association," Ehdaie said. It's possible, he noted, that HT raises the risk of clots because of its negative effects on metabolism, which can include boosting a man's fat mass.

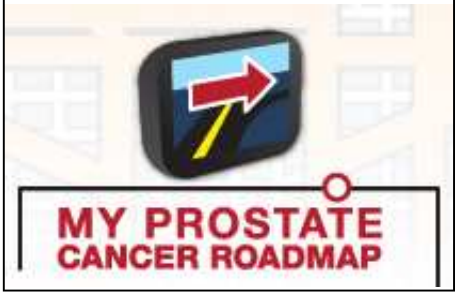
NEW CONTENT AVAILABLE ON *MY PROSTATE CANCER ROADMAP*

New content is available on the *My Prostate Cancer Roadmap* Web site, titled "*An Odyssey with Prostate Cancer: For Men Challenged by the Many Changes They Face*." This new article provides perspectives by Alan Wolkenstein, MSW, LCSW, a Senior Educator at Wolkenstein and Associates, LLC, who currently sees patients struggling to live with and through serious illness. Having received a prostate cancer diagnosis 15 years ago, Wolkenstein frequently draws on his experiences navigating his own personal journey with prostate cancer. In this article, Wolkenstein discusses and highlights points of reflection for men.

Wolkenstein recently teamed up with Us TOO International and Janssen Biotech, Inc. to contribute his expert insights to *My Prostate Cancer Roadmap*.

In Wolkenstein's essay, written specifically for men, he writes about his personal odyssey with the disease and offers insights gleaned from both his own journey as well as the conversations he's had with other men in similar situations. He discusses the personal transformation that living with cancer can create and highlights points of reflection throughout the essay as tools to cope.

Read more at http://www.myprostatecancerroadmap.com/information-resources/odyssey-with-prostate-cancer. And, you can visit Us TOO International's Web site, www.ustoo.org, for additional resources for men living with prostate cancer and their caregivers.



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

**"Statins can reduce the risk of fatal prostate cancer?
Come on dude (endearing 1970s vernacular)! What is the catch here?"**

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

Editors' note: *This column contains opinions and thoughts of its author and are not necessarily those of Us TOO International.*

Bottom Line: Statins (cholesterol lowering drugs) reduced the risk of dying from prostate cancer by as much as 73% in this latest U.S. study, and all types of statins showed some benefit.

I cannot believe Michigan won a BCS bowl game, and now I need to run out and buy a victory t-shirt that will be completely obsolete and worthless in a year, but who gives a hoot (sorry about the bad language)!

Anyway, you all know that through the years I have covered many stories about cholesterol lowering to reduce the risk of and the progression of prostate cancer. Now, there is a study that shows a large reduction in the risk of fatal prostate cancer[1] and it is a US study. Actually, the study is from New Jersey (Hey, my brother lives in Jersey! You from Jersey?), and it is one of the first population-based studies to just look at dying from prostate cancer and statin use.

More interesting is the fact that when researchers looked at multiple other things (call "confounders") that could explain these results such as weight, waist size, age, PSA screening, other diseases these men had…the results still pointed toward statins as the reason why men had a lower risk of dying from prostate cancer.

Interestingly, high-potency statins such as atorvastatin (Lipitor®) and simvastatin (Zocor®) [rosuvastatin (Crestor®) was not studied because it had not been on the market very long] had a greater impact in potentially reducing the risk of dying compared to low-potency statins.

The researchers concluded their article by saying that "we believe that it is now time to directly test the value of statins for inhibiting progression of prostate cancer in a randomized clinical trial."

Gee, I wonder if I agree with that statement (SARCASM ALERT!!!!). HEART HEALTHY=PROSTATE HEALTHY (repeat this saying 5 times a day for better health and then buy me a beer the next time you see me)!

Reference

1. Marcella SW, David A, Ohman-Strickland PA, Carson J, Rhoads GG, et al. Statin use and fatal prostate cancer: A matched case-control study. *Cancer*, 16 December 2011; Epub ahead of print

ASK DOCTOR SNUFFY MYERS

(Continued from page 3)

Clinical trials repeatedly show that your cancer almost certainly would be identified before it has spread if surveillance has been done appropriately. The key point is that active surveillance is done with curative intent – those that need to be cured are identified and treated. Should you need surgery, rest assured cure is likely. Eggener et al recently reviewed the outcomes for 12,000 patients with low risk disease after surgery and the 20 year cancer mortality was 0.2%.

Why not go directly to surgery? Because you will never be the same.

Your sexual function will be altered even if you are lucky enough to be potent. Your urinary function will be compromised. Surgical mortality is close to 0.5%. A randomized comparison of surgery to watchful waiting showed no survival advantage to surgery, suggesting that surgical mortality essentially equaled cancer mortality.

STATINS AND PROSTATE CANCER

(Continued from page 1)

statins do turn out to help prevent fatal prostate cancer, he and his colleagues said, previous studies have suggested they don't lower a man's risk of getting less aggressive forms of the disease.

Dr. Marcella's team didn't have data to determine whether taking a statin for longer, or starting one earlier, was more beneficial than more limited use of the drugs. They also couldn't tell if men started using statins before or after they were diagnosed with aggressive cancer.

But they did find that while newer, high-potency statins were linked to a lower risk of fatal prostate cancer, lower-potency drugs were not. That suggests it's something about the drugs themselves that lower men's chances of dying from prostate cancer, Dr. Marcella said.

Statins may protect against fatal prostate cancer through their known cholesterol-lowering effects, said Dr. Stephen Freedland, who studies prostate cancer at the Duke University Medical Center in Durham but wasn't involved in the new study. He said that cholesterol is a key nutrient for cancer cells, so lower cholesterol levels in the body could prevent more aggressive forms of cancer from developing.

But it's also possible that statins don't prevent certain cancers at all, Dr. Freedland said, and it's something else about men who take statins – for example, if they also change their diet and start exercising – that explains their lower risk of fatal cancer.

"It gets very, very tricky to sort out," Dr. Freedland added.

Reuters Health, 29 December 2011

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

Author: *Winning The Battle Against Prostate Cancer, 2011*

a2p1c2 Once again, statins are in the news as possibly benefitting men with prostate cancer. This most recent study suggested that prostate cancer patients who did not take a statin were more likely to die of cancer than men who were taking one of these drugs. This is not the first report to suggest a potential benefit of statins, but like all the others, this was not a properly controlled study to prove cause and effect. Fortunately, the authors did not make inappropriate claims and cautioned against taking a statin unless indicated for cardiovascular health.

The Bottom Line: Without a properly designed prospective study, we will never really know if statins benefit men with prostate cancer.

a3p1c3 Possibly the most important article in this month's *HotSheet* is the story about EPCA-2, once touted as a prostate cancer tumor marker that appeared far better than PSA. According to one news report in 2007, "the blood test detects prostate cancer so accurately that it may supplant PSA levels as a screening tool." Allegedly, the test was able to identify 94% of men who had cancer and 97% of men who did not have cancer. Many people lined up to get the test and the media sensationalized the discovery. Unfortunately, even at the time, these results were criticized as being "too good to be true", partly because of technical issues about the analysis. As we now know, results were invalid and the article has been withdrawn. In addition, lawsuits are pending against the researcher.

The Bottom Line: There are very important messages for patients here. First, when new research gets reported, results often appear much better than they truly are. That means we need to be patient while further testing occurs so we can learn the truth. That is exactly what happened with the PSA itself with so many proponents believing it was a great advance destined to save so many lives without first testing it properly. Sadly, we now know that the benefit is much smaller than initially believed and the harms are much greater than anyone suggested. We must continue to rely on good quality science before prematurely promoting new tests or treatments.

a4p2c2 For men who have had a negative prostate biopsy, the question becomes who and when should another be performed? One option has been to use MRI to identify abnormal areas. A study from 2010 is cited here in men with a PSA >4 ng/mL who had at least one negative biopsy. Prostate cancer was detected in 59% and 56% of the cases, respectively and most of them were considered "significant." This approach could become a reasonable option but could also be problematic if many non-life threatening cancers are found. Although the authors indicate that almost all the cancers were dangerous, it is difficult to know this is true without much longer follow-up. Still, the procedure does warrant further evaluation.

The Bottom Line: MRI guided prostate biopsy may be a useful way to evaluate men with a previously negative ultrasound-guided biopsy and a PSA above 4 ng/mL if validated with many more cases and critical analysis.

a5p2c3 Survival in men with progressive metastatic CRPC is improved with docetaxel. Some studies combined it with another drug called estramustine, which can cause more side effects. The study by Qi et al found that adding this drug produced a better PSA response but no difference in survival. There are two important points here; first, this study provides evidence that men can avoid taking estramustine and still get a similar benefit from the docetaxel alone. Secondly, this is yet another reason why PSA response is not a good way to evaluate treatments because a PSA decline is not predictive of a similar improvement in survival.

The Bottom Line: Men who are candidates for docetaxel chemotherapy do not appear to benefit from the addition of estramustine, meaning they can avoid potential side effects of that drug, which include nausea and risk of blood clots.

a7p3c2 The fact that PSA response is not a valid means to assess treatment outcome is particularly relevant for the two articles on proton therapy. In the first study, 211 men with low, intermediate, or high risk disease received this treatment. They claimed that serious toxicity was low, even though 42% of men needed treatment for urinary complaints. The greatest concern was that they defined benefit based on PSA response at two years, which does not reliably reflect long term survival.

In the second article, men treated with a combination of protons and photons from 1996-1999 were compared to men treated with BT alone from 1999-2002. The PSA failure rates did not significantly differ after an 8-year median follow-up. This is a ridiculous comparison, first because the time frames for each treatment were different, which leads to a significant risk for selection bias. Secondly, PSA response is not a reliable predictor of treatment effect. Lastly, about 80% of the men had low risk disease, which does not prove treatments are either effective or necessary in a group of men who would otherwise be ideal candidates for active surveillance.

What concerns me the most about these articles is the comment from ASTRO (the national organization for radiation therapists). Their website states, "Proton therapy, a type of EBRT, is a safe and effective treatment for prostate cancer." This is very self-serving and reflects the bias of this organization and the comment is a disservice to the public. Combining photons and protons does not prove that proton therapy alone is effective. Also, if results are only as good as BT, why not say that proton therapy offers no better safety or efficacy than BT but is much more expensive and time consuming? An objective, independent organization would never make this statement based on these two articles.

The Bottom Line: Despite hype and advertising, the long term effect of proton therapy in terms of curing prostate cancer remains UNREPORTED and until better information becomes available, men should be aware that the true benefit of this treatment is unknown.

(Continued on page 8)

THE BOTTOM LINE

(Continued from page 7)

a14p8c2 Among the potential disadvantages of RT for prostate cancer has been the increased risk of developing pelvic or bladder cancer. Multiple studies have found that risk to be higher, occurring in about 1 out of every 100 men getting this treatment. The study from Israel provides further support for this increased risk, suggesting that men are about two times more likely to get rectal cancer if they had RT compared to not getting this therapy. In this study, the stage at diagnosis was higher but it is not clear if that would also be true in the US. Nevertheless, this study further substantiates the potential risk from RT for prostate cancer. It is unclear from the abstract, what dose of RT was used for this study, but more than likely, men getting treated today are getting higher doses than administered in the past, which potentially may increase this risk.

The Bottom Line: Men who are getting informed about RT should be told that the risk of getting pelvic cancer is increased. The extent of that risk, however, is unknown for the higher doses used today and for the patients getting stereotactic, hyper-fractionated RT.

RADIATION THERAPY FOR PROSTATE CANCER INCREASES THE RISK OF SUBSEQUENT RECTAL CANCER

Margel D, Baniel J, Wasserberg N, Bar-Chana M, Yossepowitch O

Ann Surg 254: 947-50, 2011

Purpose:

To assess whether radiation therapy (RT) for prostate cancer increases the risk of metachronous rectal cancer and compare outcomes of rectal cancer after RT and surgery.

Patients and Methods:

The Israel Cancer Registry was queried to identify patients with prostate cancer and rectal cancer diagnosed between 1982 and 2005. The age adjusted standardized incidence ratio (SIR) of rectal cancer was defined as the ratio between the observed and expected (calculated) cases and compared among the following: overall Israeli male population, patients with prostate cancer treated with RT, patients with prostate cancer treated surgically. The medical records of men diagnosed with rectal cancer were reviewed and their clinical characteristics were retrieved.

Results:

Of 29,593 men diagnosed with prostate cancer, 2,163 were treated with RT, 67,62 were treated surgically and 20,068 patients were treated with either primary androgen deprivation therapy or offered watchful waiting. Of the entire study cohort, 194 (0.65%) patients were diagnosed with subsequent rectal cancer. Compared to the overall male population and stratified by treatment modality, the risk of developing rectal cancer after RT was significantly increased (SIR = 1.81, 95% CI 1.2-2.5), whereas it was not increased in those managed by surgery (SIR = 1.22, 95% CI 0.85-1.65). Rectal cancer after RT was diagnosed at a more advanced stage, translating into inferior disease specific survival.

Conclusions:

Compared to men diagnosed with prostate cancer managed by surgery, we observed an increased risk of rectal cancer in patients treated with RT. Further studies are needed to validate these findings and assess whether routine colonoscopic surveillance is warranted after pelvic RT.

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