Keynote Luncheon: Invasion of the Prostate Snatchers- Managing Primary Therapy

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I have a book which recently came out on the management of men with newly diagnosed prostate cancer, entitled Invasion of the Prostate Snatchers, an exposé on the management of prostate cancer. In many ways, I was motivated to write this book because of my patients who so often said my brother, my dad, my friend, was diagnosed with prostate cancer, then they rushed off and had an operation, and I wanted them to slow down and think about their options, but there was nothing I could. I wanted to create a tool for patients to give to the newly diagnosed folks, saying, this will give you some ideas.

I will talk on these concepts quickly, as well as on the whole biopsy and PSA controversy that is raging right now. Academia has raised serious questions about whether PSA screening should be done.

Here are a few questions. PSA screening reduces the absolute lifetime risk of prostate cancer mortality by how much? The correct answer is 0.5% reduction. The relative risk is reduced by 20%. Positive biopsy occurs in what percentage of men over age 55 with normal PSA levels? The correct answer is 20%. What percent of urologists in New York do less than ten radical prostatectomy surgeries per year? The correct answer is 80%. What type (low, intermediate, high risk) of prostate cancer has ten-year cancer specific survival rates of better than 90%? The correct answer is all of the above. Seed implants cause more what than surgery? The correct answer is urinary bother and irritation.

I. PSA Screening

The reason I can conduct a prostate cancer specialty practice being a medical oncologist is because of PSA. We do over 100 PSAs per week in our patients, probably well more than that; without PSA testing, I would not be able to be a prostate oncologist. PSA was approved in 1987 and is extremely valuable tool for monitoring cancer progress; it is certainly not perfect. It is a controversial tool for screening. There are other reasons which cause PSA elevation such as prostate enlargement as we age, recent sexual activity, laboratory errors, prostate infections, and high grade or low grade prostate cancer. The only thing we want to find is the high grade prostate cancer; we do not need to do biopsies on everybody with an elevated PSA.

We have basically doubled the amount of prostate cancer that we were finding prior to PSA. Instead of diagnosing 90,000 men per year, we are diagnosing close to 200,000 per

year. How many lives are we saving with screening? There has been approximately half a percentage decline in our risk of dying of prostate cancer over the last 20 years, and I attribute that to PSA and the early administration of treatment. The numbers are probably not as reflective of the benefit of screening because we know people are living longer, and therefore, we are at greater risk of dying of prostate cancer. There are 1.5 million biopsies done every year; men in the U.S. have a one out of two risk of being biopsied in their lifetime. Biopsies have changed the frequency of diagnosis as much or more than PSA.

The prostate is a small gland, and so, we can bracket the gland with multiple core biopsies and pick up even small prostate cancers, which we now know many of which are harmless. Of course, we can also diagnosis early forms of high grade prostate cancer which do need diagnosis and treatment. There is a 20% chance for finding prostate cancer when you biopsy men with normal PSA levels.

II. Management of Prostate Cancer for the Newly Diagnosed Patient

I would propose that rather than biopsying every individual with a slightly elevated PSA, we reflect a bit and consider other options first prior to biopsying. The rate of change of PSA is an issue. A new test called PCA-3, a urine test, can give some insight here. Digital rectal exams can be done, and ultrasound and MRI scans can be performed to show lesions in the prostate as well as a size estimate of the gland. You can also Google for Risk of Biopsy Detectable Prostate Cancer and do calculations based on your findings, looking at age, BMI, race, PSA, DRE, and PCA-3.

1. Prostate Cancer Is Not A Single Illness

The connection of different prostate cancer types, low, intermediate, and high risk prostate cancer, with the idea of different types of treatment has not been clearly communicated. People tend to think of prostate cancer as a single entity, which leads to tremendous confusion for patients. Gleason score is important, as well as density of core biopsies positive as well, in deciding how risky disease is, and very roughly, we can say Gleason less than seven is low risk, seven is intermediate risk, and greater than seven is high risk. This is summarized in an educational brochure from the Prostate Cancer Research Institute, which is available on the internet.

As a medical oncologist, I have been frustrated at the rush to surgery with low, intermediate, and high risk prostate cancer. Surgery as an option can be best argued for in intermediate risk prostate cancer. The first step in management of prostate cancer is defining the prostate cancer as low, intermediate, or high risk category.

2. Treatment Options

The next struggle which people have is deciding what type of treatment to undergo. Treatment needs to be based more on quality of life considerations that on survival. The prostate is situated anatomically in a difficult location; collateral damage with a surgical removal and radiation is common. The main concern is loss of sexual and urinary function. The chance of having major change in quality of life is huge. Radiation has a scary reputation of burning people. Radioactive seed implants which emit a small halo of radiation around the seed and keep the radiation inside the prostate have been shown to

deliver treatment far more accurately. The new surgical development is robotic prostatectomy, which has been very popular. This procedure leaves a much smaller scar; patients bounce back more quickly.

If surgery is curing people better, maybe experiencing some additional problems is justified. A retrospective analysis of studies which looked at surgical versus seed implant outcomes showed that the percentage of men with progression-free survival, at least with intermediate risk disease, appeared at least as good with seeds, if not better. A comparison of side effects among IMRT, brachytherapy, and surgery showed less incontinence, more urinary frequency and urgency, and better potency with seeds.

In addressing low risk disease, there are prostate cancer patients who do not need treatment. A study from 2003 suggested more than 90% who are diagnosed with low risk disease are getting aggressive treatment: surgical, radiation, or hormone blockade. An campaign from Canada is spearheading the concept of simply watching low risk patients. Watchful waiting is a different concept than active surveillance. The goal with the latter are to individualize therapy, whereas the goal with the former is to avoid treatment all together. Active surveillance can be done in any age group and the monitoring is very aggressive, whereas watchful waiting for older or sicker men and the monitoring is lax. Treatment timing with active surveillance, if treatment is given, is early, whereas it is late with watchful waiting. The goal of active surveillance is to cure people; with watchful waiting, it is symptom control.

A study of men who underwent surgery versus those who opted for watchful waiting, patients with intermediate to high risk disease, showed that at ten years, a 5% absolute improvement was seen in cancer specific survival among the surgery patients. In sum, that is one life saved ten years in the future for each 20 men treated. In looking at men with low risk disease, a 2005 study concluded that with early treatment at the time of progression, we would need to treat 100 men to save one life ten years in the future. Dr. Klotz performed a trial looking at active surveillance in men with low to intermediate risk disease, and the ten-year overall survival rate was 68%, with five out of 450 men having died of prostate cancer. Enhancement of active surveillance is possible with scanning. I believe active surveillance is an optimal treatment for men with low risk disease, and that men need to be encourage to monitor their disease when they meet the criteria for active surveillance.

Male Participant

I was diagnosed at age 46 and did not opt for surgery. My urologist is concerned about the rise in my PSA. Can you discuss percentage rise in PSA, and concern regarding performing multiple biopsies.

Dr. Scholz

The methodology for active surveillance is variable. At Johns-Hopkins, they biopsy people every year, which I think is excessive. Some recommendations are biopsying every four years for a 75-year-old; in a younger man like yourself, a lot of people recommend a second biopsy after a year, and if it is equally favorable, then maybe every two to three years after that. No one knows for sure. This approach has become popular because the alternatives like surgery and radiation have scary implications for your

quality of life. It is about balancing the risk of doing something, and what could happen to your quality of life versus the risk of missing something, which exists as well. You and your doctor must decide when it is time to do another biopsy. I would argue that at some point, you will need another biopsy.

Male Participant

I was puzzled with your interpretation of your slide for the intermediate risk group comparing seed radiation and surgery. Studies should address survival analysis since some people are lost to follow-up, some may have died, and thus, studies with short-term follow-up may be excellent, but long-term studies, assuming they were done well, it appeared to be systematic difference between the two groups.

Dr. Scholz

Those numbers are PSA relapse, not survival. The data I showed was disease-free survival, so if you were higher, that was better, with less relapses.

Male Participant

I had a biopsy four years ago and did not realize until mid-procedure how invasive the procedure is. Subsequently, I have read things about the possibility of how biopsying cancerous tissue can spread the disease through the body. What are your thoughts?

Dr. Scholz

I hope I expressed a concern about doing too many biopsies, but this is not because of my fears over spread of cancer, but rather there is a significant risk of bleeding, infection, hospitalization, and erectile dysfunction, besides being unpleasant, and in many cases, unnecessary. On the other hand, high risk prostate cancer does exist. We must balance risks and discuss with physician when biopsy is needed. I think PSA is a wonderful, if imperfect, tool that needs to be interpreted by experts before people go rushing into a biopsy. PSA is not the problem; the problem is doing biopsies on everybody that walks.

Male Participant

Can you speak on the long-term risks of active surveillance on a younger population?

Dr. Scholz

The problem is there are no long-term studies in younger men. A unanimous opinion at a conference a few years ago is that there should not be an age cutoff for active surveillance. This is the first time where we are using not clinical data but rather epidemiologic data to set clinical parameters, and I think this is the right thing to do because of the egregious amount of excess treatment currently going on.

Male Participant

Gleason seems to be the key determinant on whether or not treatment should be implemented. Is the science near the point where biopsy material can be evaluated to determine aggressiveness of a tumor?

Dr. Scholz

I think use of Gleason score is fine. The problem is that the biopsy is a random sampling of the gland. As imaging gets better, we will see improvements. Prostate biopsy techniques have definitely improved over the last ten years, so we are seeing less high grade cancer being missed on biopsy.

Female Participant

Molecular profiling is being done, but it has not yet been validated.

Male Participant

Have there been any studies done showing for men with lower risk disease, the progression of the disease with repeat biopsies? Have studies shown disease progression in a certain percentage of men?

Dr. Scholz

Johns-Hopkins has a great series; they biopsy every single year. Whether it is progression or they are just finally finding the cancer is the big question. I think it is probably both. I think it is mostly finding cancers that were there but we did not find them on previous biopsy. Most low grade cancer is not going to create a problem; we know that just by the numbers.

Male Participant

There are a number of genetic studies being done to identify aggressive cancers from nonaggressive cancers. Why aren't these tests being more widely utilized even if they are in early stages of research?

Dr. Scholz

I do not believe it is lack of tests, but rather things like proliferative rate and androgen receptor concentration. They are providing much more information than the Gleason score. We do not need to wait around for use of genetic tests. We already know that Gleason score and proliferative rate and androgen receptor give us a lot of information that is not being acted on anyway; everyone is just getting treatment. We do not need other fancy tests; let's just act on the information we already have.

Mr. Simons

Which brings up the core question in today's pay-for-performance standards: while many medical centers and doctors are measured by in terms of how many patients do you see an hour, how many diagnostics do you order, how many procedures do you do, what can a patient do to mitigate against an overwhelming establishment?

Dr. Scholz

Read my book. [laughter] It takes a whole book to get through this; this is complicated stuff. This is why I wrote the book to patients, not to doctors: the people that are

motivated are the patients themselves; patients want to get to the bottom and find out do they really need treatment or not?