Cancer Treatment: What's Best for You?

Active Surveillance

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I. Bridging Considerations

As a urologist and a patient in the prostate cancer age group I believe very firmly that PSA testing detects prostate cancer at an earlier stage and that it saves lives. I think you can argue how many lives are saved, how many you need to screen, and how many you need to treat, but the point is if you have you have a test that can detect the disease early on, and you detect it and treat it more men are going to be cured and fewer men are going to die of the disease. That is not proven, but it makes pretty logical sense.

I also agree, however, that the problem with PSA screening is that it doesn't distinguish between the "good cancers" and the "bad cancers". It doesn't tell you very accurately whether the cancer a man has is likely to kill him or whether he could live with that cancer and be spared the side effects of treatment. Because we don't have that better test to identify and distinguish good cancers from bad cancers, we wind up over diagnosing and over treating a lot of men.

All of the prostate cancer treatments can have profound effects on quality of life—urinary, bowel and sexual. If we are going to be over diagnosing and over treating a lot of men, we need to be honest with our patients in saying this is what you may gain in terms of life expectancy, but you may suffer one or more of these complications that may make that additional life expectancy less pleasant for you.

Is there a role for watching men closely who we think may have "good prostate cancer" with an opportunity to be treated at the earliest sign that they may have a "bad cancer" without impacting their curability?

II. Overview

I want to distinguish between watchful waiting and surveillance. I want to talk about some of the pros and cons of active surveillance, the problems of over diagnosis and over treatment of prostate cancer, the morbidity of treatment, which is frequently under stated by physicians, our own clinical trial, what the early results are without active surveillance, whether we can get some idea of which patients are likely to do well on active surveillance and which are not, the outcomes to date in men who have subsequently required treatment, and some concluding remarks.

III. Watchful Waiting Versus Active Surveillance

The old version of watchful waiting involved no surveillance strategy with palliative treatment only for symptomatic progression. Active surveillance is very different. Men are enrolled after being diagnosed with strict criteria and are followed closely with the goal of identifying men for curative treatment at the first sign of subclinical progression.

IV. Pros and Cons

The pros of active surveillance are that we know that screen-detected cancers to whatever degree are both over diagnosed and over treated. In addition, all prostate cancer treatments are associated with significant morbidity.

As far as cons, patients are worried that the window of curability may be lost by disease progression during the period of active surveillance, there are repeat biopsies every 12 to 18 months, there is a patient concern that repeated biopsies may induce cancer progression, and there is the real possibility that having biopsies done so often may cause scarring around the prostate that may make subsequent surgery more difficult.

V. Prevalence and Mortality

A newborn American male has a 16% lifetime risk of being diagnosed with prostate cancer, and one-third of men over age 60 and one-half of men over age 70 have prostate cancer. That being said, the lifetime risk of dying from prostate cancer is only about 3%. Many more men have the disease than die from the disease.

VI. Prostate Cancer Screening Trials

In the American trial, which was deeply flawed, they found no difference in overall survival or disease-specific survival in men who were screened for prostate cancer with PSA or men who were not screened. The problems with that trial are that about 50% of the men who were randomized not to be screened were screened anyway, and only 80% of the men who were supposed to be screened actually got screened. This makes it easy to understand why no difference in survival was seen.

In the European trial, there was a difference in survival of 20%, and this was a much better trial because all of the men in the unscreened arm did not get PSA tests and all of the men in the screened arm did get PSA tests. In terms of the European trial, however, it's a little difficult to conclude that PSA screening resulted in the decrease in cancer deaths in the United States starting in 1990 when PSA screening was only introduced at about that time. It was too early to have made a difference in survival. The data from the trial was extrapolated to look at what happens if you extend the periods of time out beyond eight years, and the number needed to screen and the number needed to treat both decrease. However, all of the patients in the screening trials were not selected for active surveillance. These were all comers, and the mean expectancy at age 65 is only 14 years. If you're going to treat all men for prostate cancer and you need to treat 503 with 12 years of life expectancy to save 1 life out of 18, there are a lot of men who are going to be treated unnecessarily. That wouldn't be a problem if prostate cancer treatment didn't cause side effects, but it does.

VII. Morbidity of Treatment

Dr. Eastham took the objective results of all fourteen of the cancer surgeons at Memorial Sloan Kettering's Cancer Center and asked at one year what percentage of men were cured, continent of urine and sexually potent. The cancer cure rates are as low as 85% but as high as about 95%, but if you look at the men who are cured, continent and have normal sexual function, that number in the best of hands is only 50%. These are the results that we need to tell our patients.

VIII. Randomized Trial of Watchful Waiting Versus Radical Prostatectomy

In the Bill-Axelson study, although there was a definite improvement in survival, the men in that study were not selected for active surveillance, and there was no attempt to distinguish the good cancers from the bad cancers. Seventy-five percent of men in the study had palpable cancers, and 50% of the men had a PSA greater than 10. The number needed to treat to prevent one death was 19.

IX. Northshore Trial

The criteria are very rigid for the Northshore Active Surveillance Trial; they are among the most stringent of any active surveillance trial in the world. If men progress so that they no longer meet the very rigid criteria, we recommend that they undergo treatment. The protocol is very rigid, and men are monitored very closely. In the first 15 months of the trial, 110 men have been considered for enrollment and 66 have entered into the trial.

X. Active Surveillance Clinical Outcomes

In five other active surveillance trials done internationally, about 25% of men will drop out of active surveillance within the first three years, and the most common reason is anxiety. The overall survival in spite of this approaches 100%.

One of the most mature active surveillance trials is being carried out at Johns Hopkins, and they have published several papers within the last year showing that by looking at the free PSA level and the percent involvement of any core with cancer they can predict fairly reliably those men who are going to do well on active surveillance and those men who are likely to progress. We need better markers, but this is a step in the right direction. Do men lose anything by enrolling in active surveillance? We believe that as long as they are selected appropriately and followed closely, they do not lose anything.

XI. Conclusions

In conclusion, active surveillance is different from watchful waiting in terms of strict enrollment criteria and close surveillance. The goal of active surveillance is to avoid over treatment and morbidity of treatment. Clinical outcomes are generally favorable but largely dependant on variable inclusion criteria. Risk stratification is possible based on initial and surveillance biopsies, but there is a need for improved imaging and biomarkers to predict and monitor disease progression. Pathological outcomes in men failing active surveillance who undergo radical prostatectomy are similar to men undergoing immediate

radical prostatectomy. Quality of life issues and patient personality are important considerations in making the decision of whether or not to enroll in active surveillance.