

REPORT:

NIH Active Surveillance Meeting
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Only a short while ago, a major U.S. task force recommended against PSA screening. They concluded that a vast majority of patients diagnosed with prostate cancer as a result of screening are harmed, not helped, by the treatment that follows.

What are the statistics? More than 90% of newly diagnosed patients are subjected to radical prostatectomy. The implication of the Task Force is that surgery does not benefit patients. Indeed, they cite clinical trials that they conclude prove their point, but I have voiced objections to their conclusions (in fact, I even made a very angry video on this, which can be found on my blog, askdrmyers.wordpress.com – it’s the October 19 video).

So, what’s wrong with the Task Force’s analysis?

First off, their analysis was stunningly incompetent: of the more than 50 randomized controlled trials available on treatment outcomes, they chose to use only two!

Furthermore, the two they used have well-known defects. Had they not been so intellectually lazy, the Task Force would have found clear proof that men with potentially lethal prostate cancer can be cured by surgery or radiation therapy. As a result, their analysis will condemn men to needlessly die of prostate cancer.

However, not all aspects of the Task Force analysis are wrong. A large majority of cancers detected by screening are either low or very low-risk cancers for which neither surgery nor radiation have any established benefit. Shockingly, more than 90% of newly diagnosed men (*continued on page 19*)

with low-risk prostate cancer undergo aggressive treatment, largely radical prostatectomy. Dr. Mark Scholz elegantly discusses this in his book, *Invasion of the Prostate Snatchers*, which I believe every newly diagnosed patient should read before agreeing to a radical prostatectomy.

If you do not have a radical prostatectomy for low-risk disease, what are the other options? The answer is that you can choose either active surveillance or watchful waiting. There is an emerging consensus among clinicians involved with prostate cancer treatment that these options are effective and need to be more widely used.

In response to this, NIH held a consensus conference on active surveillance in early December. I attended this meeting, and was very impressed. I believe this meeting was the ideal response to the sloppy job done by the U.S. Task Force. Presentations from the meeting are available at www.videocast.nih.gov.

Presentations

Perhaps the most important presentation was given by Timothy Wilt, who discussed the results of the PIVOT trial. In this trial, men were randomized to watchful waiting versus radical prostatectomy. The trial was dominated by men with low-risk disease (those with PSA values less than 10 ng/ml, most of whom had Gleason 6 disease).

The results were quite dramatic. Twelve years out, there were more deaths in the surgery arm. Thus, not only was there no survival benefit to surgery, but surgery was associated with worse survival! In addition, surgery was also associated with a significant worsening in quality of life issues, such as sexual and urinary function.

The second presentation was given by Laurence Klotz, from Sunnybrook Health Sciences Center in Toronto, Canada. Dr. Klotz could well be regarded as the father of modern active surveillance.

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In his presentation, Dr. Klotz reviewed the evolution of active surveillance at Sunnybrook. As he points out, there is a broad consensus that patients with a PSA less than 10 ng/ml and a small-volume Gleason 6 have a low-risk form of prostate cancer. Over time, approximately one third will develop progressing disease.

If these patients follow up with PSA, biopsy, or imaging techniques, progressing disease can be identified and surgery can be

done before the cancer is no longer organ-confined. This process of careful follow-up and aggressive intervention when needed is known as active surveillance.

In discussions of active surveillance, people often miss the point that this method is applied with a curative intent: the goal is to offer curative treatment ONLY to those who need it. Studies indicate that this seems to work well. Dr. Klotz cited eight studies with a total of 2,130 patients with a 99.7% cancer-specific survival. I like the fact that about 2/3 of the patients escape the harm of surgery or radiation therapy, while minimizing the cancer risk of the other third of patients who progress.

The latter half of Dr. Klotz's presentation focused on efforts to improve active surveillance techniques. In the past, most approaches depended on repeat prostate biopsies, often yearly. Prostate biopsies can be painful, and pose a risk for bleeding and infection.

Dr. Klotz pointed out that the use of prostate MRI imaging can dramatically reduce the need for repeat biopsies. First, MRI can be useful as a part of the initial evaluation.

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Routine TRUS-guided biopsies concentrate on the posterior (the back side of the prostate that can be felt with the DRE and is easiest to biopsy), but often miss cancer in the anterior prostate gland (the front side, away from the rectum). However, multiparameter MRI can detect cancer in the anterior gland, and do a better job of detecting intermediate- and high-risk cancers. This will likely reduce the proportion of patients who progress on active surveillance. Once the patient is on active surveillance, repeat MRI studies can reduce the risk for yearly biopsies. This works because MRI does a very good job of detecting advancing disease. In other words, if an MRI does not find a problem, there probably isn't one.

Here at AIDP (www.prostateteam.com), we have found that a color Doppler ultrasound, performed by Dr. Duke Bahn, serves the same function that multiparameter MRI does at Sunnybrook.

How does watchful waiting differ from active surveillance? Watchful waiting does not have a curative intent. There is no attempt to identify patients with progressive disease, and send them for surgery or radiation therapy. Patients are only treated when they develop symptoms.

In the PIVOT trial, the control arm was watchful waiting, not active surveillance. The favorable results of that trial suggest that there are patients who will do well without biopsies or imaging. However, at the meeting, no one presented convincing data on how to identify these patients. Extensive work is being done to see whether gene profiling can identify patients who do not need surveillance.

After attending this meeting, I think active surveillance is the best solution to the issues raised by the Task Force. It provides a mechanism that allows us to avoid subjecting low-risk patients to the harm caused by surgery or radiation therapy, while ensuring that those who need treatment receive it.

The major challenge is finding physicians who are committed to active surveillance. Most community urologists continue to favor surgery for low-risk prostate cancer – and it is certainly rare that a urologist, radiation therapist or medical oncologist would be interested in taking the time to develop an effective active surveillance program. For this reason, active surveillance will now become a major focus of AIDP as we attempt to fill this gap. ♦



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Myers was a key player in creating AZT, Suranim, and Phenylacetate while working at the National Institutes of Health.

With over 250 research papers published, Myers is one of the leading developers of today's prostate cancer canon on both the research and treatment side of the test tube.

Former Cancer Director at the University of Virginia, Myers opened the American Institute for Diseases of the Prostate (www.prostateteam.com) in 2002 to provide men with the kind of comprehensive care that saved his own life. To sign up for his free weekly prostate cancer video blog or subscribe to his monthly newsletter, visit www.prostateforum.com.