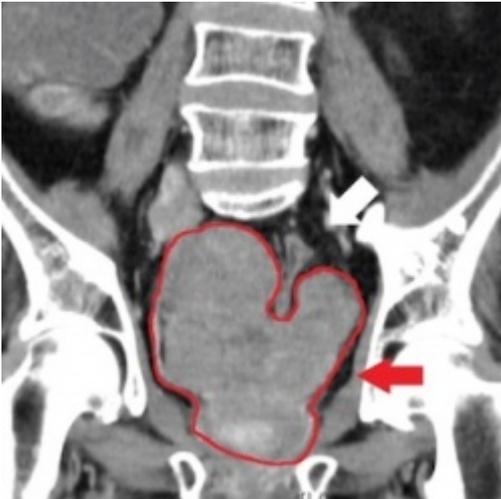


What I've Learned as a Prostate Cancer Surgeon ... and Survivor

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Credit: MR Jochumsen, et al. [1]

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Like many so-called surgeon-scientist experts in urology, I've spent my life caring for men with prostate cancer (PC) and doing research on it. However, in addition, I developed prostate cancer, had the surgery, and am cured without side effects. Actually, I'm glad I had this cancer, for it made me a more empathetic physician and a better spokesman for the disease. Finally, I was very involved in the early development of PSA.

The subject of prostate cancer is too big to cover all of it here. In passing one should know that it is the most common cancer in men: currently men have a 30% chance of getting it and a 2-3% chance of dying from it. Like breast cancer, PC is influenced by sex hormones (e.g. testosterone in men and estrogen and progesterone in women), and there is a significant hereditary factor in disease development and prognosis. Finally, like breast cancer, before efforts to diagnosis PC early, a majority of men had advanced and thus fatal disease when first detected. What we can discuss here is the controversy of PSA and screening.

But before we discuss this topic, we need to relate two issues that will enhance understanding. One is the metaphor of "turtles" and "birds". Briefly, years ago, I resurrected a metaphor that I applied to prostate cancer. Namely this cancer is like many animals enclosed in a barn yard fence. Most prominently, there are the "turtles" that grow very slowly and rarely achieve the characteristics allowing it to escape (i.e. metastasize beyond the prostate). Then we have the "birds" that, depending on growth rate and inherent characteristics, will always metastasize (e.g. spread to other organs which in prostate cancer is most often to the bone). There are also other

animals (we can group them into one animal called “rabbits”) who exhibit combinations of characteristics between “turtles” and “birds”. We’ve known for decades that there are many more turtles than birds (or rabbits) in prostate cancer. For example, for many decades we’ve known that over 70% of older men who die have the “turtle” type of prostate cancer and die never having known they had the disease. Yet there are enough “birds” in the disease that PC is the number 2 cancer killer in man.

The second issue is the phenomenology of PSA, which stands for Prostatic Specific Antigen. It is a protein that is made exclusively by normal prostate tissue but also prostate cancer. PSA is found in the blood of all normal men and most importantly in people with prostate cancer. Normal prostate cells generally make more PSA than prostate cancer cells, but it seems that PSA leaks out into the blood more with PC cells. Thus, if the prostate is removed by surgery or mostly destroyed with radiation treatment, then if PSA is found in the blood afterwards, it can only come from PC that still remains in the body. This makes PSA one of the best cancer “markers” for following disease status after initial therapies.

However, before the prostate is removed or destroyed, an “abnormal” level of PSA in the blood could either be from prostate cancer cells or from non-cancerous prostate cells rendered leakier from non-cancer causes such as infection or enlargement. This makes using PSA blood levels as an indication for a prostate biopsy and thus early detection complicated and doing “screening” (i.e. testing everybody) problematic. For example, unless the PSA level is very high (making PC almost certain), minimally elevated PSA levels are usually not from prostate cancer.

Despite these draw backs, widespread use of PSA and better methods for prostate biopsy were adopted by the urology community with the hope that this approach (i.e. screening) would pick up the cancer early and reduce cancer deaths. Subsequently there was a tremendous surge in the number of men diagnosed with early prostate cancer. Also, the death rate from PC and the percent of men who had advanced disease when diagnosed plunged.

As expected, the side effects of aggressive “local” treatment (e.g., impotence, urinary, and bowel problems) soared. Accordingly, many “turtles” were picked up and many of those patients were treated unnecessarily. Also, even eventually fatal prostate cancer often takes many years before death. Thus, because PC is a cancer of older men, many who are diagnosed with PC ended up dying of something else. So randomized studies testing whether early diagnosis was beneficial showed many people with side effects and initially an advantage to screening that was relatively small.

There is a government sponsored committee called the U.S. Preventive Services Task Force (USPSTF). One of its functions is to assess and “grade” methods of cancer screening. In 2012, when they looked at the early data from the randomized studies, they assigned PC screening a D grade; that is, they recommend *against* screening because they felt the side effects greatly outweighed the survival benefit.

A great outrage ensued among physicians who took care of PC patients warning that the PC death rate would catastrophically rise. Yet in retrospect, this seemingly mistaken recommendation had benefit because it galvanized physicians to accelerate their use of conservative treatment. To over-

simplify, this involved avoiding diagnosing PC in older men (e.g. over 70) or younger, sick men with a life expectancy less than 10 years. For younger, healthier men in which PC is diagnosed, doctors carefully watched for “turtles” and treated only if the patients subsequently showed signs of more aggressive disease.

Thanks to the widespread adopting of active surveillance and the fact that analysis of the randomized studies later in follow-up showed significant additional survival benefit, in 2018, the USPSTF changed their mind and gave PC screening a C rating. This means that men younger than 70 should first be counseled about the risks and benefits of screening, but also offered the opportunity for early diagnosis and aggressive treatment where appropriate.

This new grade designation was greatly applauded by those physicians involved in PC care, but most still consider it not ideal. While counseling is essential, most of us believe that encouraging men to aggressively diagnose PC is important between the ages of 45-70. Those below 45 who have a strong family history of PC should also consider early diagnosis. In fact, recent evidence suggests that men with a family history of breast or ovarian cancer should also consider earlier PC diagnosis. Over age 70, the situation should be individualized and diagnosis might be appropriate in men in excellent health. Importantly, those whose cancers seem to be “turtles” should be encouraged to be treated with active surveillance.

There are those who think that the data for breast cancer screening is no better than PC screening, but tradition and political considerations have influenced the USPSTF to give better B and C ratings depending on age. Some critics of breast cancer screening suggest that the dramatic reduction in breast cancer deaths with the implementation of mammography is due more to better treatment than earlier diagnosis.

In fact, that hypothesis is probably also operational in PC; that is, early diagnosis and aggressive treatment when appropriate not only cures significant numbers of men, but in those men who progress nonetheless, the application of better “systemic” treatments that are now available, extends life considerably and thus decreases the men who die from the cancer. Most importantly, amazing recent progress in PC research has encouraged many experts (including yours truly) to expect that this cancer will be cured or at least adequately controlled within their lifetimes.

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