

PROSTATE CANCER UPDATE: 2106

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Prostate cancer is the most common non-cutaneous malignancy diagnosed in men. Last year in the U.S. an estimated 240,000 men were diagnosed with the disease, and 29,000 died because of prostate cancer. Approximately one in six men will be diagnosed with prostate cancer in their lifetime.

Over the last five to 10 years we have seen dramatic changes in the way prostate cancers are detected and treated. Traditionally, prostate cancer was detected using PSA testing and digital rectal exam with the primary treatments being surgery and/or radiation. For metastatic disease, patients were treated with hormonal therapy and cytotoxic chemotherapy. In this article we will discuss what's new in prostate cancer screening, diagnosis, and treatment of localized and metastatic disease.

Screening

The PSA (prostate specific antigen) blood test is the most widely used screening test for prostate cancer since it first came into use in 1994. Men who are screened for prostate cancer using PSA are more likely to find their cancers earlier and have a higher chance of cancer cure. It is, however, not a perfect test, and many patients and physicians question its role in prostate cancer screening.

First, a PSA test can give both false-positive and false-negative readings. Men with normal PSA readings may have prostate cancer, a false negative. More commonly, men with high PSA readings do not have cancer, a false positive. Men with high readings but without cancer go through unnecessary prostate biopsies and follow-up testing.

Second, prostate cancer in many men is indolent. PSA screening detects non-lethal as well as lethal cancers. One of the key challenges is differentiating those cancers which can be followed via active surveillance and those potentially aggressive cancers that will lead to significant morbidity and mortality. Most experts agree that not every prostate cancer needs to be treated. A significant trend clinically has been the acceptance by patients that not all cancers need immediate, aggressive treatment.

Controversy regarding PSA testing increased substantially after the U.S. Preventative Services Task Force came out with its position statement in 2010, giving the PSA blood test a "D" rating as a screening tool. Although many urologists and oncologists were critical of the rating, many practitioners at the primary care level drastically changed their discussion with patients and practice patterns regarding PSA testing. Patients also became more critical of the test after heavy publicity of the USPSTF rating.

In 2013, the American Urologic Association established its own guidelines. The AUA does not support the USPSTF position on PSA screening. The AUA recommends the omission of PSA screening for men with a life expectancy less than 10 years or those under 40. For all other men the AUA advocates shared decision-making for men and their physician regarding PSA testing; especially those men between ages 55-70 or those with a strong family history of disease.

Shared decision-making relies heavily on the guidance of a medical practitioner looking out for the best interest of the patient. We would encourage you to review the AUA guidelines at: www.auanet.org/education/guidelines/prostate-cancer-detection.cfm

As urologists we strongly advocate for prostate cancer screening. In 2015 the current standard is the PSA test; in the future we hope a more cancer-specific test will emerge.

Diagnosis

The PSA is a basic screening test. It is often a starting point with patients as we discuss whether to perform a prostate biopsy, and, if a cancer is found, whether treatment or surveillance is most appropriate. Here we have also seen advances.

There are new genetic and biomarker studies which have added to our ability to find prostate cancers.

Examples include the PHI (Prostate Health Index) or a 4Kscore- measures 3 or 4 different types of PSA kallikreins in the blood, and the PCA3; a urine test that looks for a protein that is produced by prostate cancer cells. These tests are used to predict risk of high grade cancer prior to a patient having a biopsy. Advances in genetic testing allow us to better determine which cancers should be treated. Examples of this include the Oncotype DX and Prolaris-genetic tests run on a biopsy specimen to help determine if the biopsy sample represents low or higher risk disease.

Recent advances in MRI of the prostate have improved our ability to identify prostate cancers and, in some cases, differentiating indolent from aggressive tumors. Urologists traditionally use trans-rectal ultrasound as a guide during a prostate biopsy, but the ultrasound is a low-resolution image. We now have software that can fuse a fixed MRI image with real time ultra-sonography. The radiologists reading the MRI will draw out specific areas requiring biopsy; the urologist can "fuse" that image with the ultrasound and insure that those specific areas are biopsied. This sequence creates a more targeted biopsy, detecting cancers we may have otherwise missed.

Treatment of Localized Disease

There is an increasing interest in active surveillance for low-grade prostate cancers. Active surveillance is a close monitoring process that typically involves frequent PSA testing and rectal exams, repeat prostate biopsies, and imaging studies such as MRI to try to detect

progression of disease. While active surveillance is gaining traction, the gold standard for treatment of prostate cancer remains radical prostatectomy. Over the last decade daVinci robotic radical prostatectomy has emerged as the preferred surgical approach in the overwhelming majority of hospitals and centers of excellence. Robotic prostatectomy has shortened recovery times, decreased blood loss and, in experienced hands, improved outcomes.

Radiation, brachytherapy seed placement, cryotherapy (freezing), and a recently FDA approved treatment, high-intensity focused ultrasound (HIFU), are also options for treatment of localized prostate cancer. Traditionally we treat or remove the entire prostate, even the benign tissue.

A different and developing strategy is focal therapy. Using some of the newer technology such as HIFU or cryotherapy we can ablate only the cancerous lesion while leaving the normal prostate intact. While focal therapy is not yet considered standard of care, improving imaging with MRI and other means of identifying the tumor location within the prostate will likely make focal therapy a more common and standard option in the near future.

Treatment of Advanced Disease

Prostate cancer is hormone sensitive and creating castrate levels of testosterone can help control the disease. Androgen deprivation therapy (ADT) uses either surgical castration, medical castration, and/or combined androgen blockade with the use of anti-androgens.

Despite initial tumor response to ADT, most cases will become resistant over time. Historically once the cancer became castrate resistant (CRPC) the only options were cytotoxic chemotherapy. Newer treatments have shown improved survival.

Abiraterone acetate (Zytiga) and Enzalutamide (Xtandi) are second-line inhibitors of androgen activity in the body either by reducing production (Zytiga) or by androgen receptor blockage (Xtandi). Both are being used commonly by urologists and oncologists for treatment after failure of initial ADT. Both show very good response and extension of survival.

Sipuleucel-T (Provenge) was a first of its kind cancer vaccine. It involves the autologous infusion of patient's own blood cells after they are exposed to the prostate cancer antigen in a lab. It has been shown to extend overall survival as well.

Radium 223 (Xofigo) is a radioactive agent used to target bone metastases. It is especially useful for men with late stage, painful bony metastatic disease.

Conclusion

The landscape of prostate cancer diagnosis and treatment continues to evolve and improve. We believe this will help the lives of the many men diagnosed with prostate cancer. As urologists who are part of a larger practice, Metro Urology, that focuses on prostate cancer we see the benefit of adopting and employing these new technologies. We are excited about the future of prostate cancer care.

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