To screen or not to screen? A case of prostate cancer not seen and a patient not heard Jeanette Goldwaser, MD

Story from the frontlines

A 50-year-old man presented to his primary physician for a preventive visit. A prostate-specific antigen (PSA) test was ordered for prostate cancer screening, with a resulting value of 27. The patient had no symptoms to suggest underlying prostate cancer. He was referred to urology where the decision was made to perform a prostate biopsy, the pain from which the patient would recount for years to come. The biopsy revealed "fibromuscular and adipose tissue, specimen inadequate for diagnosis." Urology recommended a repeat biopsy and, after a discussion outlining the risks of missing a potential case of prostate cancer, the patient refused because of the degree of pain he experienced with the prior biopsy. A decision was made to monitor PSA levels every 6 months and to perform annual bone scans to indirectly monitor for malignancy. Fourteen years later, the patient has undergone a total of thirteen bone scans, all of which have been normal, and twenty PSA tests, the values of which have ranged from 11 to 38. Discussion with him this year uncovered his wish for no treatment should he have prostate cancer, a preference that he revealed he has had for some time.

Teachable moment

The value of PSA screening for prostate cancer is controversial. Prostate cancer's position as the second leading cause of cancer death among men in the United States and the prospect of early detection and treatment via the PSA has historically made prostate cancer screening commonplace. But as the harms of PSA testing have become better known, the enthusiasm for routine PSA testing has decreased with organizations such as the American Academy of Family Physicians discouraging its use a screening test¹. This case offers a rare, personal glimpse into the perils of PSA testing.

An enzyme released by prostate cells, PSA elevation in the serum is observed in prostate cancer. However, elevations are seen in other more common conditions including benign prostatic hyperplasia, prostatitis, or mechanical force to the prostate resulting from activities as mundane as bicycling. As a result, false positives are common with PSA testing. The decision to screen should take into account several variables, including the patient's life expectancy, risk of prostate cancer death and desire for testing after consideration of the benefits and harms of screening. Three systematic reviews on PSA screening have demonstrated no benefit for all-cause mortality, though the data on prostate-cancer specific mortality is mixed.^{2,3,4} The ERSPC trial which included 162,243 men aged 55-69 years found a modest prostate cancer-specific mortality benefit at median 13 year follow-up, with a number needed to invite to screening of 490-1,929.⁵ This finding was not reproduced in the CAP and PLCO trials, which found no prostate-cancer specific mortality benefit.^{6,7}

The decision to screen must weigh the potential for reduced prostate cancer mortality against the harms of PSA testing. This case brings to light the risks of prostate biopsies including pain, infection, bleeding, urinary retention, hospitalization, which occurred in 17% of patients at 30-days per a retrospective cohort study of 104,584 men.⁸ Added to the litany of complications are the more severe effects associated with the prostate cancer treatment which may ensue from a positive biopsy. Further complicating this analysis is the relatively high prevalence of prostate cancer, which may be indolent, especially in men with limited life expectancy. A systematic review of 29 case series including 8,776 men who died of non-prostate cancer-related causes

found that 59% of men over the age of 79 and 15% of men aged 40-50 had prostate cancer on autopsy. This data calls into question the need to treat, let alone diagnose, all prostate cancers and lends support for the now commonly chosen management strategy of "active surveillance" for lower risk prostate cancer. It also raises the important issue of overdiagnosis which is the identification of cancer that if left alone would never lead to symptoms or death. Best estimates of overdiagnosis among PSA detected prostate cancers range from 20-50%. ¹⁰

In the face of such complexities surrounding the risk-benefit analysis of PSA testing, the importance of shared decision-making cannot be overstated, as this case demonstrates. Though it is unknown whether a discussion was had with the patient regarding his desire for treatment at the onset of testing 14 years ago, a recent discussion uncovered the patient's disinterest in pursuing treatment in the event that he has prostate cancer. A five minute discussion with the patient revealed the clinical and financial futility of several years and thousands of dollars' worth of testing, while elucidating a clear future plan of care deferring ongoing testing. Shared decision-making is a key element of curbing unnecessary PSA testing, as too often the decision to screen is unilateral.

¹ Choosing wisely. September 24, 2013; updated July 18, 2018.

² Fenton et al. JAMA. 2018 May 8;319(18):1914-1931.

³ Ilic et al. BMJ. 2018 Sep 5;362:k3519.

⁴ Ilic et al. Cochrane Database Syst Rev. 2013 Jan 31;(1):CD004720.

⁵ Schroder et al. N Engl J Med. 2009 Mar 26;360(13):1320-8.

⁶ Andriole et al. N Engl J Med. 2009 Mar 26;360(13):1310-9

⁷ Martin et al. JAMA. 2018 Mar 6;319(9):883-895.

⁸ Gershman et al. Eur Urol. 2017 Jan;71(1):55-65.

⁹ Bell et al. Int J Cancer. 2015 Oct 1;137(7):1749-57.

¹⁰ US Preventive Services Task Force. Screening for Prostate Cancer: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2018;319(18):1901–1913.

¹⁰ Bell et al. Int J Cancer. 2015 Oct 1;137(7):1749-57.

¹⁰ US Preventive Services Task Force. Screening for Prostate Cancer: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2018;319(18):1901–1913.