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Editorials

EARLY STAGE PROSTATE CANCER—DO WE HAVE A PROBLEM WITH OVER-DETECTION, OVERTREATMENT OR BOTH?

We have seen profound changes in prostate cancer presentation and treatment during the last 20 years. Mortality rates are decreasing, and whether this is the result of improved early detection methods or treatment strategies is a matter of debate. What is clear is that the disease we most often see today is not the disease urologists saw 20 years ago. Widespread and repeated use of serum prostate specific antigen (PSA) and prostate biopsy has resulted in a profound stage (risk) migration. Approximately 90% of prostate cancers detected today are clinically localized. This fact is even more remarkable compared to the clinically localized rate at detection of other common cancers such as breast (63%), cervical (55%) and colorectal (39%). If one were to define risk more completely using serum PSA, cancer grade and cancer stage, all important measures of tumor behavior, the proportion of patients with favorable or low risk tumor characteristics has risen from 29.8% in 1989 to 1992 to 45.3% in 1999 to 2001 ($p < 0.0001$).[1] This trend is accelerating today as we increase the number of biopsy cores taken and lower the serum PSA threshold for biopsy.

The cancers we are finding are significantly smaller, of lower stage (most not palpable or stage T1C) and generally amenable to curative treatment using current available technology, usually surgery or radiation. However, some have argued that such an achievement has come at a price of increasing the risk of over-detection, that is detecting a cancer that would not become clinically apparent during the lifetime of the patient if left untreated. The risk of over-detection has been estimated to be between 16% and 56%. Such estimates are based on the definition of over-detection, the age at which screening occurs and the frequency of testing. Estimates from the European Randomized Study of Screening for Prostate Cancer suggest that for a screening program with a 4-year screening interval from age 55 to 67 the estimated mean lead time is 11.2 years (time from detection to the cancer becoming clinically apparent) and the over-detection rate is 48% (range 44% to 55%).[2]

Given the increasing numbers of men with low risk disease, do all of them need immediate and/or aggressive treatment? This question brings up another problem. In this country detection and treatment are tightly linked. If prostate cancer is detected at any stage, grade or volume in almost any age group it is almost uniformly treated. Are at least some of these men candidates for active surveillance? Interestingly, despite the increasing numbers of men with favorable disease characteristics, prostate cancer treatment patterns appear to be more aggressive today compared to those of a decade ago.[3] The rates of watchful waiting have declined significantly.[4] Even more remarkably, it appears that the majority (75%) of men 75 years old or older with low risk disease are treated rather than considered good candidates for active surveillance. Treatment no matter how "minimally invasive" or expertly done is usually costly and accompanied by some trade-offs with regard to health related quality of life.[5] Such trade-offs are acceptable to those men at significant risk of dying of disease but may be less acceptable to those who may never know they had the disease if it were not for a biopsy.

To date, most patients opting for watchful waiting have been older with more comorbidity or strongly averse to current treatment alternatives. Initial watchful waiting trials reported on study populations with higher clinical T stage, PSA and Gleason scores, and found that metastasis developed in several men during prolonged observation.[6] However, with the development of better monitoring algorithms, new trials are exploring the possibility of offering safe initial observation to greater numbers of patients.[7] Urologists either uncomfortable or unfamiliar with such studies should read this growing body of literature. Patients who have low risk tumor characteristics (as defined by serum PSA and its variations, cancer grade and extent of cancer on extended pattern biopsy), especially those of more advanced age, could pursue a trial of initial active monitoring at the time of diagnosis without sacrificing curative intent or exposure to undue risk of disease progression. Such an approach could preserve quality of life and achieve substantive cost savings without significantly impairing cure rates. Many have demonstrated the feasibility of "active surveillance." Such patients, if well selected and monitored, do not appear to sacrifice the ability to be effectively treated at a later date. Clinicians and patients considering active surveillance should understand that under grading and under staging could occur and that the disease could be of a higher grade and volume. However, such risks are minimized with the use of a well performed extended pattern prostate biopsy, an essential component of initial and ongoing risk assessment. Under staging and significant under grading are not the problems today that they were 2 decades ago.

Urologists should be aware that the controversy over these issues (over-detection and overtreatment) extends far beyond our specialty. Increasingly, such issues are presented and discussed in high profile journals or conferences where the vast majority of the readership or audience, respectively, are not urologists. In addition, the lay press has taken up these issues as evidenced by a recent story in the *Wall Street Journal* of a 32-year-old man with early stage prostate cancer contemplating treatment (which he has delayed).[8] Over-detection and overtreatment are problems and we should only question their magnitude.

The field of urology will be judged on how we treat prostate cancer now and in the future. As a specialty we need to acknowledge that these problems exist and we, not another specialty or government agency, should deal with them primarily. We should begin by unlinking detection and treatment, as they are separate processes. Our zeal for immediate and aggressive treatment of such early cancers should be matched, if not exceeded, by an enthusiasm for identifying better markers of the need for treatment and carefully conducted trials of surveillance in well selected and monitored men. We should identify a future path that is evidenced based, focused on the issues that make a difference to patients, and results in better and longer lives of those with the disease and those who are at risk of getting it. If that path leads to an end where we treat fewer patients (although

likely some more aggressively), we should pursue it with energy and confidence.

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1. Cooperberg, M. R., Lubeck, D. P., Mehta, S. S. and Carroll, P. R.: Time trends in clinical risk stratification for prostate cancer: implications for outcomes (data from CaPSURE). J Urol, **170:** S21, 2003
2. Draisma, G., Boer, R., Otto, S. J., van der Cruijsen, I. W., Damhuis, R. A., Schroder, F. H. et al: Lead times and overdetection due to prostate-specific antigen screening: estimates from the European Randomized Study of Screening for Prostate Cancer. J Natl Cancer Inst, **95:** 868, 2003
3. Cooperberg, M. R., Lubeck, D. P., Meng, M. V., Mehta, S. S. and Carroll, P. R.: The changing face of low-risk prostate cancer: trends in clinical presentation and primary management. J Clin Oncol, **22:** 2141, 2004
4. Harlan, S. R., Cooperberg, M. R., Elkin, E. P., Lubeck, D. P., Meng, M. V., Mehta, S. S. et al: Time trends and characteristics of men choosing watchful waiting for initial treatment of localized prostate cancer: results from CaPSURE. J Urol, **170:** 1804, 2003
5. Wei, J. T., Dunn, R. L., Sandler, H. M., McLaughlin, P. W., Montie, J. E., Litwin, M. S. et al: Comprehensive comparison of health-related quality of life after contemporary therapies for localized prostate cancer. J Clin Oncol, **20:** 557, 2002
6. Johansson, J. E., Andren, O., Andersson, S. O., Dickman, P. W., Holmberg, L., Magnuson, A. et al: Natural history of early, localized prostate cancer. JAMA, **291:** 2713, 2004
7. Allaf, M. E. and Carter, H. B.: Update on watchful waiting for prostate cancer. Curr Opin Urol, **14:** 171, 2004
8. At 32, a decision: is cancer small enough to ignore? The Wall Street Journal. Monday, December 20, 2004