PSA Testing and Overdiagnosis: Can Computers Sort This Out?

Etzioni R, Penson DF, Legler JM, et al. Overdiagnosis due to prostate-specific antigen screening: lessons from U.S. prostate cancer incidence trends. J Natl Cancer Inst 2002;94:981–90.

Study Overview

Objective. To measure the extent of prostate cancer overdiagnosis due to prostate-specific antigen (PSA) screening.

Design. Computer simulation model.

Model. A computer simulation model of PSA testing and subsequent prostate cancer diagnosis and all-cause mortality was developed. The model used a hypothetical cohort of 2 million men in the United States who were between the ages of 60 and 84 years in 1988. The projected incidence of prostate cancer associated with PSA testing was compared with the observed incidence of prostate cancer in the United States from 1988 through 1998. The model incorporated PSA testing rates, rates of prostate cancer detected by screening, lead time (the time in which PSA testing advances the diagnosis of cancer), and the secular trend (ie, projected cancer incidence that would have been expected in the absence of screening). PSA testing and screen-detected prostate cancer rates were obtained by matching the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) registry with Medicare claim files from the Health Care Financing Administration (HCFA). Men diagnosed with prostate cancer before PSA testing occurred were excluded from analysis. Lead time was estimated from values used to generate the expected prostate cancer incidence that best matched the observed SEER incidence. The secular trend was estimated to parallel the incidence of prostate cancer detected as a result of transurethral resections of the prostate over the same period. Finally, the age distribution and age-specific all-cause mortality rates for the cohort were derived from census data.

Main outcome measures. Overdiagnosis rates, with overdiagnosis defined as the fraction of cases of prostate cancer detected through PSA testing that otherwise would not have been diagnosed within the individual's lifetime.

Main results. Mean lead times of 5 years and 7 years were most consistent with the observed prostate cancer incidence rates from the SEER data for white and African-American men, respectively. SEER data on prostate cancer incidence from 1988 through 1998 were consistent with overdiagnosis rates of 29% for white men and 44% for African-American men with prostate cancer detected by PSA screening. Secular trends strongly influenced which combination of lead times and overdiagnosis rates were most consistent with the observed incidence of prostate cancer from SEER data.

Conclusion. The observed trends in prostate cancer incidence are consistent with considerable overdiagnosis among PSA-detected cases. Still, the majority of screen-detected cancers diagnosed between 1988 and 1998 would have presented clinically, whereas a minority of cases found at autopsy would have been detected by PSA testing.

Commentary

The incidence of prostate cancer in the United States rose threefold to 244,000 new cases diagnosed in 1995 compared with a decade earlier [1]. Few would dispute that most of this increase was due to the widespread use of PSA testing. However, many continue to debate the appropriate role of PSA screening. Aside from the cost considerations of mass testing (particularly in an older population), no well-designed randomized controlled studies have shown a reduction in disease-specific mortality or morbidity as a result of PSA testing [2]. Perhaps of greater concern is the potential risks related to testing, such as treatment-related morbidity and effects on quality of life.

Etzioni et al designed a computer model to help examine the extent of prostate cancer overdiagnosis due to PSA testing. Appreciating that the National Cancer Institute's U.S. Prostate, Lung, Colon, and Ovary Screening Trial and the European Randomized Study of Screening for Prostate Cancer will take a number of years to yield results, this analysis attempts to quantify overdiagnosis by comparing model-projected incidence with the observed incidence from a national cancer database. The simulation concludes that the overdiagnosis rates, while not small, comprise a minority of screen-detected cases.

How are we to interpret these results? Etzioni et al help demonstrate the complexities involved in assessing cancer incidence following a screening test. Their model incorporates

several key factors: PSA testing rates, rates of prostate cancer detected by screening, lead time, and secular trend. While many of these values were based, as the authors point out, on "reasonable assumptions," it is important to consider the potential hazard of making presuppositions. Projecting the expected cancer incidence in the absence of screening (secular trend) is difficult at best and yet stongly influences the overdiagnosis rates in the model.

Another important consideration is how overdiagnosis is defined. The authors chose to examine the proportion of men diagnosed by screening who otherwise would not have had cancer detected clinically in their lifetimes. The study's definition diverges from historical and more common definitions that describe overdiagnosis as detecting cancer in men who otherwise would have remained asymptomatic, which is well discussed in an accompanying editorial [3]. Because clinically detectable (asymptomatic) prostate cancer can precede symptomatic disease by many years, Etzioni et al shorten the period of time an overdiagnosis can be made—that is, the time in which a diagnosis could be made but an individual dies from an unrelated cause.

A diagnosis of prostate cancer most often leads to an intervention. Advances in radiotherapy (external beam or brachytherapy) and radical prostatectomy have made treatment safer (and hopefully more effective) but still come at a considerable risk of morbidity in terms of incontinence, hematochezia, and impotence. Even if this study's overdiagnosis rates are skewed downward, there is still a significant number of men who may be overdiagnosed. Arguing that more men will be diagnosed who would otherwise have had clinically evident or symptomatic disease remains unsatisfying at a time when there are no conclusive data on the optimal treatment for early-stage disease.

Applications for Clinical Practice

Prostate cancer screening remains a challenging topic because of remaining questions regarding the benefits of testing and risks of treatment. Making a diagnosis of a cancer that may not affect a patient's overall mortality or quality of life exposes that patient to significant potential risks. Computer modeling can be a useful approach to analyzing complex issues related to screening while we await the results of prospective randomized studies.

–Review by David R. Spigel, MD

References

1. Boring CC, Squires TS, Tong T. Cancer statistics, 1996. CA Cancer J Clin 1996;46:5–27.
2. Bullock AD, Andriole GL. Screening for prostate cancer: prostate-specific antigen, digital rectal examination, and free, density, age-specific derivatives. In: Kantoff P, Carroll PR, D'Amico AV, editors. Prostate cancer: principles and practice. Philadelphia: Lippincott, Williams & Wilkins; 2002:195–211.
3. Yao S-L, Lu-Yao G. Understanding and appreciating overdiagnosis in the PSA Era. J Natl Cancer Inst 2002;94:958–60.

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