Less Is More
Prostate Cancer: Doing Less Might Be More

The phrase “out of sight, out of mind,” as suggested by Nicolas Bruchovsky,1 aptly describes the fact that while no other organ causes so much illness in man as the prostate, so little is known about its role in the body. And yet, with our aging population, a lifetime risk of death from prostate cancer of 3%, and dramatic (ie, 2-fold) increase in a lifetime risk of a diagnosis of prostate cancer owing to PSA screening, prostate cancer represents one of the most challenging issues facing physicians today.

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Over the past several decades, PSA screening of asymptomatic men for prostate cancer has come to represent an accepted “truth” in the medical community on the assumption that this test should be innately beneficial, following the concept that, as with other common malignant conditions including colorectal and breast cancer, earlier diagnosis is associated with a lower potential for occult established metastases and a higher potential for cure by local therapeutic means. Though attractive for prostate cancer, this concept frequently does not work out in clinical practice,2 and unfortunately, the hope of early beneficial diagnosis has contributed to overdiagnosis and overtreatment of prostate cancer with attendant life-altering morbidities including high rates of post-therapeutic bowel, bladder, and sexual dysfunction. Appreciation of these facts and the slow natural history (growth) of many prostate cancers has redirected attention to life expectancy, quality of life considerations, and comorbidities as key factors in clinical decision making for patients with prostate cancer, as considered by Daskivich et al in this issue of the Archives. Twenty years ago, even prior to widespread use of PSA testing, life expectancy and comorbidities were shown to be key and independent factors in evaluating clinician decision making among men with prostate cancer.3

We would be remiss in attributing the present failure of the potential beneficial effects of PSA screening and the resultant overdiagnosis and overtreatment of prostate cancer to the concept of “screening.” “Screening” is scientifically sound but only if the subsequent use of a single (or multiple) cancer-specific marker(s) can distinguish between the 2 types of prostate cancer: those that will kill you and those that will not. Although the specificity of PSA for the prostate makes it a very useful clinical tool as a harbinger for recurrence of prostate cancer following treatment,4 because PSA is not cancer specific, it cannot detect prostate cancer and cannot be a screening test for dangerous prostate cancer in the manner the PSA test is currently used, and, ipso facto, it will never be a tool that can distinguish the dangerous from the nondangerous cancers, ergo, the failure of PSA screening.5

Prostate cancer is the most heterogeneous of cancers, and we cannot approach any case as representative of all. Linking PSA to treatment without proper risk stratification of the cancer that is diagnosed and without sufficient consideration of comorbidities, quality of life preferences, and life expectancy will mean that PSA will likely cause more harm than good. Therefore, in concert with PSA’s absence of cancer specificity and with prostate cancer being an age-related disease, a PSA-prompted biopsy will find cancer in approximately 25% of men between the ages of 60 and 69 years.6 If one looks carefully at prostate specimens obtained at autopsy among men in this age group, the percentage of men with prostate cancer is approximately 65%.7

Prostate cancer is much akin to a turtle and a rabbit in an open box. The “turtle,” a non–life-threatening cancer, wanders around the box, while the “rabbit,” a potentially life-threatening (killer) cancer, hops around and might jump out of the box and metastasize. Finding a rabbit early on (while still in the box) affords the opportunity to cure a cancer that might otherwise lead to the death of the patient. The question is, how many turtles are there for every rabbit? We are uncertain of the exact answer, but the available evidence suggests that the turtles are common and that the rabbits are not. With the use of Gleason scores, studies have indicated that approximately 85% of men harbor tumors with a biopsy Gleason sum of 6 or lower, representing turtles rather than rabbits.5 Thus, PSA screening, as presently used, has resulted in overtreatment and overdiagnosis of millions of men whose cancer would have never metastasized and who would have died from something other than prostate cancer in most cases.

Against this backdrop, we believe that accurate assessment of the characteristics of the prostate cancer (Gleason scores, clinical stage, number of positive biopsy results, and the percentages of cancer in the positive cores), as well as the life expectancy, comorbid conditions, and quality of life concerns of the patient, become ever more paramount to any clinical decision making for prostate cancer and most notably in the selection of aggressive and potentially morbid treatment in young men with early-stage disease. Therefore, we agree with and strongly support the concept of “active surveillance” for many men with early-stage disease, particularly in the presence of comorbid conditions and among men with relevant and important concerns over potential bladder, bowel, and sexual dysfunction. We believe that physicians who do not offer and perform active surveillance in a significant number of patients with localized disease should strongly reconsider their position in light of the articles in this issue of the Archives and other recent data and should counsel their patients that active surveillance deserves to be considered at least as strongly as aggressive therapy for the majority of patients with prostate cancer.

By way of example, a recent trial involving 453 men undergoing active surveillance over a period of 13 years disclosed that a man’s risk of dying from prostate cancer was 1% vs the 16-fold-greater risk of death from another condition.8

For men who are being “actively surveilled,” there are still concerns regarding both undertreatment and overtreatment. Particularly noteworthy regarding the use of PSA was the observation that “PSA triggers” (ie, a predetermined increase in PSA level) for radical treatment of men with prostate cancer who are being actively surveilled for nonprogressive disease included a false PSA trigger recommending unacceptable rates of treatments as high as 84%.9

The impact of increases of PSA levels after local therapy for prostate cancer, ie, biochemical recurrence considered in the article by Uchio et al10 in this issue of the Archives, raises similar concerns regarding false PSA triggers for treatment. In this study, most patients with biochemical recurrence after radiation therapy or surgery did not die from prostate cancer. Prostate-specific antigen kinetics, however, are extremely helpful. For example, in the data from the Hopkins database,11 patients with rapid PSA doubling times of less than 3 months were at very high risk of prostate cancer death, and those with slow doubling times of 15 months or more were at very low risk of prostate cancer death. Only in the group with a PSA doubling time of less than 15 months did more deaths occur from prostate cancer than from other causes.11 Treating all patients with PSA recurrence after surgery or radiation therapy will lead to overtreatment in a significant percentage of patients. Those at lowest risk of death include those with increased age or multiple comorbidities.

Given our present state-of-the-art testing for the diagnosis and treatment of prostate cancer, the lesson, when possible, is that doing less may be more for the majority of patients we diagnose and for many patients with recurrent prostate cancer after local therapies as well.

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Lack of Improvement in Outpatient Management of Congestive Heart Failure in the United States

Congestive heart failure (CHF) accounts for 3% of admissions to US hospitals, and the diagnosis carries a mortality rate of 20% at 1 year and 80% at 8 years.1,2 Numerous advances in the chronic medical management of CHF, including angiotensin antagonists, β-blockers, and aldosterone antagonists, have significantly reduced mortality in clinical trial populations with varying degrees of CHF severity.3-5 Practices proven in clinical trials, however, do not always readily translate to community practice.6,7 Previous studies in outpatient populations in the late 1990s through the early 2000s observed suboptimal adoption of evidence-based therapy for CHF. Using nationally representative data, we evaluated whether patterns of medication use have improved.

Methods. We used data from the National Disease and Therapeutic Index (NDTI) physician survey produced by IMS Health (Plymouth Meeting, Pennsylvania) to characterize contemporary trends in the outpatient use of recommended medications for CHF from January 1994 through March 2009. Estimates for 2009 are made using data from January through March 2009. The NDTI is an ongoing physician survey that provides nationally representative diagnostic and medication use information on patients treated by office-based, private practice physicians in the continental United States.

We used descriptive analyses to determine the proportion of visits where the use of selected medication classes was reported. For the NDTI estimates, 95% confidence intervals (CIs) were calculated using tables of relative standard errors that accounted for the complex, multistage NDTI sampling design.

Results. The number of patient visits for CHF declined gradually over the 15-year study period, from 10.9 million nonhospital visits in 1994 to 8.5 in 2000 and to 5.7 million visits in 2008. Physician-reported degree of CHF severity for patient visits did not change appreciably over time. Angiotensin-converting enzyme inhibitor (ACEI) or aldosterone II receptor blocker (ARB) use gradually increased from 34% (95% CI, 32%-36%) in 1994 to 45% (95% CI, 43%-46%) in 2002 (Figure). However, after 2002, there was a steady decline in ACEI or ARB use, decreasing to 32% (95% CI, 27%-33%) in 2009. Because ARB use remained steady after 1998, fluctuating between 4% and 9%, the trend in ACEI and ARB use was entirely due to the rise and fall in ACEI use for CHF. We observed a gradual increase in β-blocker use for outpatient CHF visits from 11% (95% CI, 9%-12%) in 1998 to a peak of 44% (95% CI, 42%-46%) in 2006. After 2006, there was a decline in β-blocker use to 37% (95% CI, 31%-40%) in 2009.

There was a slow increase in aldosterone antagonist use in CHF from 1% in 1998 to 11% in 2003, maintaining a fluctuating plateau through 2009 (range, 8%-12%). A stable proportion of patients with CHF was reported to be receiving treatment with digoxin from 1994 to 1997 (range, 39%-43%), with a substantial decline after 1997 to 32% in 1999, to 20% in 2004, and to 10% in 2009. The use of diuretics declined slowly over 15 years from 69% in 1994 to 56% in 2009.

Comment. Initial adoption of evidence-based therapies for CHF through the 1990s and mid-2000s was modest. What we observe after the mid-2000s is more troubling. Some therapies that previously were increasing slowly have reached a plateau. Other recommended therapies have declined. The persistence of this trend could lead to a regression in the beneficial outcomes achieved through the increasing use of these therapies. The current framework used to promulgate evidence-based therapy for CHF does not appear to be sufficient to facilitate appropriate levels of therapy. Our results suggest that further improvements in the adoption process are needed, perhaps through targeting at-risk patient sub-