Androgen Deprivation as Primary Treatment for Early Prostate Cancer: Should We “Just Do Something”?

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In few diseases are treatment options as distinct, consequences as enduring, and the supporting data as uncertain as for early prostate cancer. The abrupt general acceptance of prostate-specific antigen (PSA) screening a decade ago doubled the number of men diagnosed annually (1,2) and brought the average age at diagnosis forward an estimated 5 years (so-called lead time) (3). The increased incidence, earlier diagnosis, and prostate cancer’s usually indolent natural history, further magnified by another effect of screening—length-biased sampling—resulted in an estimated 1.4 million U.S. prostate cancer survivors in 1998 (Surveillance, Epidemiology, and End Results [SEER] Program data: http://cancercontrol.cancer.gov/ocs/prevalence). Five-year survival rates for all prostate cancer patients rose from 80% in 1986 to 97% in 1993, the most recent patients’ cohort with 5-year SEER data. Yet no randomized trial comparing any of the primary treatment modalities for early (nonmetastatic) prostate cancer—radical prostatectomy, external-beam radiation therapy, brachytherapy (radioactive seed implants), or observation—has been completed in the past 20 years. Most men develop severe, permanent erectile dysfunction after any local treatment, and enduring urinary incontinence or bowel symptoms, depending on the treatment modality, are common (4–7). Tens of thousands of men make treatment decisions with very little help from medical research that will ramify for years.

The absence of trial data has not prevented large changes in treatment practice patterns. Two decades ago Walsh and colleagues (8) found that avoiding transection of periprostatic neurovascular bundles lessened the previous certainty of postprostatectomy impotence, and the frequency of this operation increased sixfold from 1984 to 1990 (9). Subsequent attention to patient selection and perhaps a growing appreciation of the risks of urinary incontinence and erectile dysfunction and of the importance of selecting appropriate patients (4,5,10) dampened en-
Deprivation therapy (ADT) for men with asymptomatic early prostate cancer with androgen deprivation therapy (ADT) (13). The PCOS, a large population-based cohort study, has provided vital new information to clarify men’s experience after the diagnosis of prostate cancer (14–18). By randomly sampling recently diagnosed patients in six registries of the SEER Program, it obtains much more generalizable results than the convenience samples studied elsewhere, includes the growing proportion of patients under age 65 invisible in otherwise representative Medicare-based samples and, by oversampling minority populations, provides crucial new information on understudied populations carrying the heaviest disease burden. However, it is not without flaws. Even using Rapid Case Ascertainment, most patients are identified 4–6 months after diagnosis, when treatment has usually begun and is often complete. To obtain a baseline necessary to identify the deficits due to treatment, the PCOS investigators asked patients to recall their precancer state, allowing time to erode and the experience of treatment to bias their recollected self-assessments, especially if their pretreatment function was abnormal. The PCOS study demonstrates why population-based cohort studies are rare: convenience samples are more convenient to study. Participation in the PCOS surveys was lower (62% of their sample) and the dropout rate higher (18% of men who completed the first 6-month survey did not complete the 12-month survey) than that for other reports, largely because socioeconomically disadvantaged patients are sicker, harder to locate, and less receptive to research.

This report focused on the 701 (23%) of 3073 patients with early (nonmetastatic) cancer who did not undergo surgery, radiation, or cryotherapy for their cancers. Excluding 40 patients for whom the timing and thus the purpose of androgen ablation was unclear, 661 patients did not receive any localized, potentially curative initial treatment. The study’s first surprising finding was that 245 (37%) of these men underwent ADT alone for their primary therapy, an indication authoritatively endorsed nowhere in the medical literature. The patients’ survey responses showed that they paid a price in symptoms. Compared with men who were simply observed, men who underwent ADT were more than fivefold more likely to report breast swelling and hot flashes and, if they reported pretreatment potency, more than twice as likely to become impotent. General measures of health showed that they paid a price in symptoms. Compared with men who were simply observed, men who underwent ADT were more than fivefold more likely to report breast swelling and hot flashes and, if they reported pretreatment potency, more than twice as likely to become impotent. General measures of health showed that they paid a price in symptoms. Compared with men who were simply observed, men who underwent ADT were more than fivefold more likely to report breast swelling and hot flashes and, if they reported pretreatment potency, more than twice as likely to become impotent.

And thusiasm for surgery, especially for older men. However, dissemination of a new percutaneous technique for delivering radiation to the prostate—radioactive seed implantation or brachytherapy—was so rapid that a 20% radical prostatectomy decrease in men over 65 between 1993 and 1997 was completely offset by increased brachytherapy (11). And, as the most recent result from the National Cancer Institute’s Prostate Cancer Outcomes Study (PCOS) in this issue of the Journal by Potosky et al. (12) confirms, during the last decade physicians began to treat men with asymptomatic early prostate cancer with androgen deprivation therapy (ADT) (13).

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REFERENCES


NOTE

1Editor's note: SEER is a set of geographically defined, population-based, central cancer registries in the United States, operated by local nonprofit organizations under contract to the National Cancer Institute (NCI). Registry data are submitted electronically without personal identifiers to the NCI on a biannual basis, and the NCI makes the data available to the public for scientific research.