Further Perspectives on Treating Localized Prostate Cancer

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Standard treatment options for prostate cancer patients include surveillance, surgery, external-beam radiotherapy, brachytherapy, the combination of external-beam and brachytherapy, and the combination of radiotherapeutic modalities with hormonal therapy, for appropriately chosen patients.

Unfortunately, randomized data comparing these treatments are limited, which makes the determination of relative efficacy and toxicity problematic, as is made clear in Drs. Ciezki and Klein’s paper. Their institutional treatment outcome analyses reaffirm that comparing biochemical control between surgical and radiotherapeutic treatment modalities is problematic, in part, due to differences in standard definitions of biochemical failure among the modalities.

**Low vs Intermediate Risk**

In the absence of demonstrated differences between surgery and radiotherapy in cancer control rates, other considerations such as logistics (eg, convenience of the treatment process) and toxicity profiles influence the choice of prostate cancer care modality. For many younger men with low-risk or the lower end of intermediate-risk disease, the 2-month time commitment of daily radiation treatments may appear onerous compared to the single outpatient visit of brachytherapy. Surveillance, on the other hand, can be difficult for patients to accept due to uncertainty as to whether a cancer’s suitability for cure will change over a potentially long course of follow-up. In this context, young men with low-risk prostate cancers often gravitate toward surgery or brachytherapy, despite a paucity of direct evidence supporting these options over external radiotherapy or active surveillance in the setting of low-risk prostate cancer.

For patients with intermediate-risk disease, treatment with surgery or external-beam radiotherapy is standard and is supported by survival benefits observed in randomized clinical trials. The use of brachytherapy as monotherapy is commonly practiced, condoned by clinical practice guidelines,[1,2] and the topic of an ongoing Radiation Therapy Oncology Group (RTOG) clinical trial for selected intermediate-risk patients. Eligibility for the RTOG trial is limited to patients with clinical stage T2b disease, or lower, and either Gleason ≤ 6 with prostate-specific antigen (PSA) 10 to 20 ng/mL, or Gleason 7 with PSA < 10 ng/mL). In this trial, patients are randomized between brachytherapy alone or a combination of external-beam radiotherapy and a brachytherapy boost. Comparative cancer control and quality-of-life outcomes from this trial will not be available before a projected accrual completion in 2011, but the trial results will hopefully help guide treatment decisions thereafter.

**Quality of Life**

In terms of long-term side effects, brachytherapy and surgery can each affect erectile or urinary function, while the former can also occasionally affect bowel function. Several papers published in the past 10 years have used validated survey instruments to evaluate the toxicities caused by the different treatment modalities,[3-5] and relative outcomes have been consistent with Drs. Ciezki and Klein’s observation that surgery patients had worse scores for sexual function and urinary continence at 2 years, while brachytherapy patients had worse scores for rectal irritation and urinary irritation/obstruction (which were actually improved in surgery patients).

Many articles evaluating health-related quality of life (HRQOL) report averages of respondent HRQOL questionnaire “scores,” which are useful for quantitative analyses but can be difficult to apply to medical decision-making for individual patients. However, HRQOL outcomes can also be presented as the frequency of specific levels of morbidity before and at defined time points after treatment. Although of limited utility for quantitative analysis, such presentation of HRQOL outcomes provides a
transparency that can facilitate the use of these data to counsel patients regarding outcome expectations.

For example, based on HRQOL data from the Prostate Cancer Outcomes and Satisfaction with Treatment Quality Assessment (PROST-QA) study, one can infer that among men with good erectile function prior to treatment, after 2 years 25% to 30% of them will have erectile dysfunction if treated with brachytherapy, compared with 45% to 50% after prostatectomy. For urinary continence—depending on how continence is defined—3% to 6% of men will have treatment-induced incontinence 2 years after brachytherapy, as will 6% to 20% of them after prostatectomy. What is underappreciated is the fact that prostatectomy can actually benefit HRQOL, as it led to improvement in urinary irritation or obstruction in 7% to 8% of patients, while brachytherapy caused additional obstructive urinary symptoms in 4% to 10% of treated patients at 2 years. In addition, after brachytherapy, 5% to 6% of treated patients had worse bowel function than before treatment, primarily manifest as rectal urgency and frequency.

Discerning how these different HRQOL domains ought to weigh in decisions regarding treatment requires careful attention to baseline symptoms and lifestyle priorities: Does a patient have problematic obstructive urinary symptoms from concurrent benign prostatic hyperplasia? Is he disinterested in sexuality, or is the ability to have intercourse paramount? Attention to such concerns can simplify decisions that in a less granular view may seem challenging to navigate.

**Need for Predictive Models**

A large number of factors will have an impact on an individual patient’s likelihood of disease control and of developing treatment-related morbidity. In addition to risk category (low, intermediate, or high), the chances of cancer control and treatment morbidity may each be modified by the extent of the primary tumor, prostate size, medical comorbidities, and prostate cancer treatment details (eg, nerve-sparing during surgery, details of brachytherapy, or effects of practitioner expertise in either setting). There is a practical need for predictive models to be developed that account for these factors as well as for pretreatment baseline symptoms in order to individualize risk assessment as an aid to patient decision-making.

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