Guideline for the Management of Clinically Localized Prostate Cancer: 2007 Update

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INTRODUCTION

In December 1995, the AUA published the *Report on the Management of Clinically Localized Prostate Cancer*.[1] The document was the culmination of six years of work by 17 clinicians and scientists and required the evaluation of 12,501 scientific publications with the detailed extraction of information from 165 papers that met the rigorous criteria of the panel of experts (Appendix 1 on-line). The Panel noted that a lack of evidence precluded specific recommendations for optimal treatment of an individual patient, which patients should be offered all treatment options, and that patient preferences should guide decision making.

Since 1995, approximately 2,600,000 men[2] in the United States have been diagnosed with prostate cancer, and nearly 375,000 men[3,4] have lost their lives to this disease. In addition, the National Cancer Institute[4] has spent $2.1 billion on prostate cancer research and as of November 2005, approximately 28,111 scientific papers concerning prostate cancer have been published in peer-reviewed medical journals (OVID Search, December 31, 1995 to October 23, 2005; key word: prostatic neoplasms). At the same time, mortality rates from prostate cancer have been declining: 34,475 men died in 1995 compared with an estimated 30,350 in 2005.[4] Several pivotal RCTs related to prostate cancer treatment have been completed, including a chemoprevention study,[5] along with studies demonstrating prolongation of life in men with hormone-refractory metastatic disease[6,7] and improved outcomes in men with nonmetastatic disease.[8–35] With the use of new and combined treatments, the frequency and variety of complications have differed from those previously reported. Advances have been made in prostate cancer imaging, biopsy methodology, in understanding causative factors and disease, in treatment-related QOL and in predicting the behavior of individual tumors using risk strata.

Despite these advances, no consensus has emerged regarding the optimal treatment for the most common patient with prostate cancer: the man with clinically localized stage T1 to T2 disease with no regional lymph node or distant metastasis (T1 to T2N0-NxM0). Of the 234,460 men in the United States diagnosed with prostate cancer annually, 91% have localized disease.[36] For these men and their families, the bewildering array of information from scientific and lay sources offers no clear-cut recommendations.

Understanding this challenge for patients with newly diagnosed localized prostate cancer and the explosion in research and publications, the AUA re-impaneled the Prostate Cancer Clinical Guideline Panel (Appendix 2 on-line) for the purpose of reexamining and updating its analysis of treatment options. We herein report the results of a 5½-year effort to update the 1995 Guideline. The online version of this Guideline, which can be accessed at http://www.auanet.org/guidelines/, contains appendixes that include additional documents used in the conduct of the analysis and the graphics detailing the Panel's findings.

CONTEXT

A contemporary man with localized prostate cancer is substantially different from the man with prostate cancer of 20 years ago. With the advent of PSA screening beginning in the late 1980s and the dramatic increase in public awareness of the disease, the average new prostate cancer patient has generally undergone multiple prior PSA tests and may

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For another article on a related topic see page 2352.

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even have experienced one or more prior negative prostate biopsies. When the cancer is detected, it is in a substantially earlier stage, often nonpalpable clinical stage T1c with, perhaps, one to several positive biopsy cores. The typical patient usually is very familiar with his PSA history and has a history of multiple visits to either his primary care provider or urologist. The most common patient will likely have Gleason score 6 or 7 disease, reflecting the most common current grading category and the fact that contemporary uropathologists assign this score more often than in the past when this group of tumors was frequently diagnosed one or two scores lower.[37] The average patient of today also will more commonly have serum PSA levels in the 4 to 10 ng/mL range, and often in the 2.5 to 4.0 ng/mL range. In many cases, the patient's PSA history will include sufficient data to allow a prediagnosis PSA velocity or doubling time to be calculated. Generally, the treating physicians will personalize the patient's risk based on serum PSA level, highest/worst Gleason score, clinical stage, and burden of disease (either number or percent of biopsy cores with cancer).

Following diagnosis, today's patient will oftentimes be better informed and consequently request a second opinion by other physicians including other urologists or such specialists as radiation and medical oncologists. Many centers offer multidisciplinary clinics where the patient can consult with urologists, and with radiation and medical oncologists at one location. After considering the options and gathering several opinions, a patient and his family will choose among active surveillance, interstitial prostate brachytherapy, EBRT, and RP with treatment generally commencing two to three months after diagnosis. Aside from this complex decision, where the evidence basis for action has been suboptimal, patients now also are faced with subtle but important technical decisions such as choosing the type of surgery (eg open vs laparoscopic/robotic prostatectomy), the type of radiotherapy (eg conformal vs intensity modulated), the type of brachytherapy isotope, or whether a combination (eg brachytherapy and EBRT) of therapies should be used. Minimal data currently are available for the following interventions: high-intensity focused ultrasound, cryotherapy, high-dose rate interstitial prostate brachytherapy, and primary hormonal therapy. Conclusions regarding outcomes of these treatments cannot be made.

It is in this very changed environment that we present the 2007 AUA Prostate Cancer Clinical Guideline Panel report.

DEFINITIONS AND TERMINOLOGY

The reader desiring a greater degree of information regarding the terminology used herein is directed to Appendix 3 on-line, which provides a glossary of terms important to a full understanding of the management options of localized prostate cancer.

Screening Tests

Clinically localized prostate cancer generally causes no symptoms. Slowing of the urinary stream, arising at night to void, and increased urinary frequency are common symptoms associated with aging but often are unrelated to the presence of prostate cancer. It is for this reason that early detection tests have been developed to identify prostate cancer while it remains confined to the prostate. The two most commonly used tests are a serum PSA level and a DRE.[38,39]

PSA

Prostate specific antigen is a protein produced by cells within the prostate, and in men PSA can be measured in the blood. While higher blood PSA levels often are noted in men with prostate cancer, PSA elevation is not specific for prostate cancer. At present, a higher PSA test value is the most common reason why prostate cancer is detected in the United States.

DRE

A DRE is an examination by a physician using a gloved finger placed into the rectum to feel the surface of the prostate. The region of the prostate adjacent to the rectal wall is where tumors commonly develop; hard regions or asymmetry may indicate the presence of prostate cancer.

Prostate Biopsy

Although a higher PSA value or abnormal DRE may raise the suspicion of prostate cancer, detection requires confirmation with a prostate biopsy. At the time of biopsy, several small cores of tissue are removed from the prostate and are then examined by a pathologist to determine if cancer is present.

Tumor Characteristics

Tumor grade. Tumor aggressiveness can be determined by the pathologist's examination of the microscopic pattern of the cancer cells. The most commonly used tumor grading system is the Gleason grading.[40,41] This system assigns a grade for each prostate cancer from 1 (least aggressive) to 5 (most aggressive) based on the degree of architectural differentiation of the tumor. Tumors often show multiple different grade "patterns" within the prostate or even a single core biopsy. To account for this, the Gleason score is obtained by assigning a primary grade to the most predominant grade present and a secondary grade to the second most predominant grade. An exception to this is in the case where the highest (most aggressive) pattern present in a biopsy is not either the most predominant or second most predominant pattern; in this situation, the Gleason score is obtained by combining the most predominant pattern grade with the highest grade. The Gleason score is then displayed as, for example, 3 + 4 where 3 would be the most common pattern of tumor and 4 the second most common pattern (or highest pattern) of tumor seen in the core. Given that the individual Gleason value can range from 1 to 5, the added values (Gleason scores or "sums") can range from 1 + 1 to 5 + 5 or from 2 to 10. Generally, Gleason scores of 2 to 4 are uncommon; as a result, the majority of detected tumors range from 5 to 10.

Occasionally, if a small component of a tumor on prostatectomy is of a pattern that is higher than the two most predominant patterns, then the minor component is added as a tertiary grade to the report (eg 60% pattern 3, 35% pattern 4, and 5% pattern 5 should be reported as 3 + 4 with tertiary grade 5).

High-grade cancer. With each increase in tumor score (eg from Gleason 5 to 6), there is an increase in tumor aggres-