An Overview of Prostate Cancer: Diagnosis and Treatment

Dawn Mielke Strief

Prostate cancer is the most commonly diagnosed cancer and the second leading cause of cancer-related death among American males (Terris & Rhee, 2006). The incidence of this disease is highest among Caucasian and African-American males, with reported incidences of 140/100,000 and 222/100,000, respectively (U.S. Department of Health and Human Services [DHHS], 2006). The incidence of prostate cancer is 40%, yet mortality rates are reported as 3% (Bott, Birtle, Taylor, & Kirby, 2003). Thus, while there is a high incidence of the disease, early, effective, and appropriate treatment positively impacts outcomes.

Many health care professionals will care for individuals with prostate cancer, or know individuals at risk for developing prostate cancer. Thus, familiarity with the guidelines for screening, treating, and managing early or localized prostate cancer should be known by all nurses.

The state of the science for prostate cancer is presented including a review of current screening, diagnosis, and treatment options for localized prostate cancer. Educational resource options appropriate for this population are outlined.

STAGES OF PROSTATE CANCER

Localized prostate cancer has been defined as a cancer confined to the prostate (Bott et al., 2006). To date, research has failed to link prostate cancer to any specific modifiable lifestyle choices, but has identified non-modifiable risk factors. These include increasing age, a family history of the disease, and ethnicity. Higher incidences of localized prostate cancer are reported among men over age 60, especially those who are African-American (DHHS, 2006). Caucasian men have the second highest incidence of prostate cancer and rates of this disease are lowest among men of Asian-American and Hispanic-American decent (DHHS, 2006). The American Cancer Society (2006) estimates that one in six men will be diagnosed with prostate cancer during their lifetime, but only 1 in 34 will die of this disease.

The fact that family history has been identified as a major risk factor for prostate cancer has resulted in much research to identify a genetic component (Lessick & Katz, 2006). The first prostate cancer susceptibility gene, HPC1 (Hereditary prostate cancer 1), was discovered in 1996 (Smith et al., 1996) and mapped to the long arm of chromosome 1. Since then, several other prostate cancer susceptibility genes have been linked to various regions on other chromosomes (Ostrander, Markianos, & Stanford, 2004; Verhage & Kiemeney, 2003).

In addition to the discovery of the HPC1 gene, several other theories have been developed in an attempt to explain the genetic basis of prostate cancer. The Mendelian autosomal dominant inheritance theory is thought to best explain familial clustering of prostate cancer among men with early-onset disease (Verhage & Kiemeney,
2003). Approximately 43% to 65% of prostate cancer cases diagnosed before the age of 56 have been linked to the presence of a rare, autosomal dominant high-risk susceptibility gene (Verhage & Kiemeney, 2003). A multifactorial model has been developed which describes how prostate cancer may occur when several susceptible genes interact with environmental factors (Gong et al., 2002).

Recently, a virus was identified which may be an environmental factor that influences the development of prostate cancer. The HPC1 gene has been implicated in viral defense and scientists have found that men with mutations in their HPC1 gene harbor this virus 30 times more than men without the genetic mutation (Hampton, 2006). The HPC1 gene encodes an antiviral protein which is activated by viral infection. Any impairment in this gene has been proposed as a susceptibility factor in the development of prostate cancer (Hampton, 2006). There has been speculation that the virus interacts with the prostate and the tissue surrounding it to cause prostate cancer. Further research in this area is aiming to develop a vaccine to prevent prostate cancer (Simard et al., 2003).

Prostate cancer frequently has no specific clinical symptoms. Lower urinary tract symptoms may be present, but these are neither specific nor sensitive enough to diagnose prostate cancer. Lower urinary tract symptoms are more specific to another condition known as benign prostatic hyperplasia (BPH) and should not be directly correlated to the presence of prostate cancer. However, if prostate cancer is present, lower urinary tract symptoms may also be present, especially if the prostate enlarges or intrudes into the urethral space. Lower urinary tract symptoms may include urgency, hesitancy, frequency, dysuria, weak stream, and urine leakage. In a review article, Hamilton and Sharp (2004) determined that lower urinary tract symptoms are more prevalent in the presence of prostate cancer, yet the high prevalence of these symptoms among the general population decreases their predictive value. Therefore, there is no evidence that lower urinary tract symptoms are associated with localized prostate cancer and the presence of these symptoms are not sensitive or specific enough to aid in the diagnosis of prostate cancer.

At present, there are no symptoms that are specific to the diagnosis of prostate cancer. Rather than rely on symptoms, patients should have routine prostate cancer screening, which includes a digital rectal examination (DRE) and obtaining a blood sample to determine the presence of the prostate-specific antigen (PSA). If one or both of these screening examinations are abnormal, further investigation should occur. Intervention at this stage allows prostate cancer to be detected early, when it may be localized and treatment may cure or control.

**DIAGNOSTIC WORK-UP**

**Screening**

PSA is an enzyme created only by prostate cells (Stutzman, 2003). Elevated levels of PSA have been positively correlated with prostate cancer, but are not specific for prostate cancer. Elevated levels of PSA are also seen in the presence of BPH, prostatitis, prostate abscess, manipulation of the prostate, prostatic infection, and ejaculation within the previous 48 hours (Stutzman, 2003). Thus, screening only by PSA results has been met with some controversy.

The variability of PSA results within an individual further complicates PSA testing and contributes to the continuing controversial nature of the test. Research by Soletormos and associates (2005) determined that there are biological variations of total prostate-specific antigen (tPSA). These researchers determined that while tPSA is increasingly used for screening, diagnosis, and monitoring of prostate cancer, serial measurements of individual tPSA levels varied by more amplitude than could be accounted for by the analytical variation of the test. It was hypothesized that this variation was caused by intra-individual variation. Further research must be performed to determine if the variation of tPSA is greater in men with known prostate cancer, when compared to those who do not have this disease. It appears that the biological variation of tPSA is 20% and is influenced by age. Thus, using this laboratory value to screen or follow treatment is not a certainty.

In addition to the biological variation associated with tPSA levels, the accuracy of the PSA test should be explored. The Physicians’ Health Study, performed by Gann and colleagues in 1995 (Harris & Lohr, 2002), used longitudinal followup data rather than biopsy to determine the sensitivity and specificity of the PSA test. Analysis of these data determined that the sensitivity for PSA in detecting prostate cancer within 2 years was 73.2%. The specificity of the PSA test was 85.4% among men who did receive a diagnosis of prostate cancer within 2 years. These data also determined that the specificity of the PSA level is lower among men with large prostate glands, a population which includes men with BPH. These researchers concluded that prostate cancer screening using the PSA test is not appropriate among men with BPH, since the PSA level would be falsely decreased. The results of this study have led experts to suggest that PSA levels be adjusted for age and decreasing the abnormal PSA level from 4.0 ng/mL to 2.6 ng/mL (Gretzer & Partin, 2003).

Digital rectal examinations are also used as a screening mechanism for prostate cancer. In a meta-analysis, Harris and Lohr (2002) determined that the sensitivity of this test was 59% and its specificity was undeterminable. Thus, while this procedure may be useful in detecting prostate cancer among those with a low PSA, the limited reproducibility of the examination limits its clinical significance.
Prostate cancer screening may result in a false-positive response. This may result in unnecessary and invasive testing. Therefore, the net benefit of prostate screening activities remains controversial. Further research needs to occur with respect to appropriate screening activities, the meaning of the results, and when further diagnostic and treatment activities are warranted.

**Diagnostic Examinations**

Usually, men with prostate cancer have a PSA result higher than 10 ng/mL (Berger et al., 2007). It is rare for men with BPH to have such an elevated PSA level. Men who have a PSA serial increase in 1 year of 0.75 ng or more over baseline PSA should undergo further screening. This rate of change is known as PSA velocity, and has been associated with and specific for the diagnosis of localized prostate cancer (Berger et al., 2007). If asymptomatic, an elevated PSA should be correlated with a DRE. If these results create a suspicion for prostate cancer, a referral should occur, and a prostate biopsy performed. If positive, the cancer should be staged using the Gleason Scoring System, the Tumor, Nodes, Metastasis (TNM) classification, or the Whitmore-Jewett staging system (Stutzman, 2003).

**Gleason Scoring System**

The Gleason Scoring System separates the cancer diagnosis into five different histologic grades (Stutzman, 2003). Grade 1 tissue is well-differentiated and provides the best prognosis. Treatment for individuals with a Grade 1 tumor may result in a cure. Poorly differentiated cancers are classified as Grade 5 and carry a poor prognosis. These individuals require extensive treatment, with an appropriate treatment goal being tumor control. Tissue samples are obtained from two different sites, with the grade for each tissue sample defined separately and the two scores added. The highest Gleason score possible is 10, if each site obtains a grade of 5. Prostatic intraepithelial neoplasia (PIN) may also be identified in the biopsy tissue. PIN is known to be a premalignant lesion for prostate cancer and these individuals have an increased risk for prostate cancer in subsequent biopsies (Stutzman, 2003).

**Tumor Staging Classifications**

Stage A (T1, N0, M0) prostate cancer is disease that cannot be palpated during DRE of the prostate (Stutzman, 2003). This stage is further divided into T1a and T1b. T1a is well-differentiated and involves less than 5% of the prostate gland. T1b is also well-differentiated yet involves more than 5% of the prostate gland. This determination is often made when performing a surgical procedure for symptoms of BPH. Stage T1c indicates that the prostate gland was biopsied as a result of an elevated PSA level (Stutzman, 2003).

Stage B (T2, N0, M0) is limited to the prostate gland and is usually found by DRE in which a nodule or hardness may be palpated. Stage T2a is defined as the presence of a palpable node which involves up to one-half of one lobe. Stage T2b is defined as a palpable lesion which involves more than half of one lobe, but not both lobes. Stage T2c describes a palpable node, present in both lobes.

Stage C (T3 and T4, N0, M0) is local-extensive prostate cancer (Stutzman, 2003). This stage has a palpable node and unilaterial capsular penetration. Stage T3a describes a palpable node which has bilaterally extracapsular extension. Stage T3b involves a palpable node which has invaded the seminal vesicles. Stage T4 involves a palpable node which has invaded adjacent structures, such as the bladder neck, sphincter, rectum, or pelvic wall. The inclusion of N or M in the staging describes a cancer that has metastasized to the lymph nodes and distant metastases (such as bone), respectively (Stutzman, 2003).

**Staging Classifications**

Stage A (T1, N0, M0) prostate cancer is disease that cannot be palpated during DRE of the prostate (Stutzman, 2003). This stage is further divided into T1a and T1b. T1a is well-differentiated and involves less than 5% of the prostate gland. T1b is also well-differentiated yet involves more than 5% of the prostate gland. This determination is often made when performing a surgical procedure for symptoms of BPH. Stage T1c indicates that the prostate gland was biopsied as a result of an elevated PSA level (Stutzman, 2003).

Stage B (T2, N0, M0) is limited to the prostate gland and is usually found by DRE in which a nodule or hardness may be palpated. Stage T2a is defined as the presence of a palpable node which involves up to one-half of one lobe. Stage T2b is defined as a palpable lesion which involves more than half of one lobe, but not both lobes. Stage T2c describes a palpable node, present in both lobes.

Stage C (T3 and T4, N0, M0) is local-extensive prostate cancer (Stutzman, 2003). This stage has a palpable node and unilateral capsular penetration. Stage T3a describes a palpable node which has bilaterally extracapsular extension. Stage T3b involves a palpable node which has invaded the seminal vesicles. Stage T4 involves a palpable node which has invaded adjacent structures, such as the bladder neck, sphincter, rectum, or pelvic wall. The inclusion of N or M in the staging describes a cancer that has metastasized to the lymph nodes and distant metastases (such as bone), respectively (Stutzman, 2003).

**Whitmore-Jewett Staging**

The Whitmore-Jewett Staging classification is similar to the TNM classification (Stutzman, 2003). Stage A is a clinically undetectable tumor, usually found incidentally. Stage A1 is focal and well-differentiated. Stage A2 is diffuse or poorly differentiated. Stage B is limited to the prostate upon rectal examination. Stage B1 implies one solitary node, less than 1.5 centimeters, and involves only one lobe. Stage B2 involves one whole lobe or both lobes. Stage C extends locally outside of the prostate capsule or into the seminal vesicles. Stage D implies metastatic disease while Stage D1 involves pelvic lymph node metastases and Stage D2 involves distant metastases (Stutzman, 2003).

**TREATMENT OPTIONS**

**Watchful Waiting**

Watchful waiting, or active surveillance, involves routine observation of a client’s prostate cancer clinically and undergoing routine PSA testing. According to a review article by Bott and associates (2003), a link exists between Gleason scores and PSA levels at time of diagnosis to rate of progression. Higher grades of prostate cancer increase the risk of metastases and death. The risk of having a known prostate cancer progress, other health care concerns, and comorbidities, along with other demographic data that may place this person at risk for disease progression, should be included when this treatment is selected.

**Radical Prostatectomy**

This surgical procedure requires the entire prostate gland be removed, along with the seminal vesicles and usually the obturator lymph nodes. These nodes are obtained for cancer staging purposes. Surgical approaches can include a transperineal route, a laparoscopic approach, or a transurethral resection of the prostate. Each approach has obtained similar outcomes, but the transperineal
approach may be accomplished with less blood loss, no abdominal incision, and decreased pain (Bott et al., 2003). There are two downsides to this approach. One is that lymph node sampling is not possible and will require an additional procedure. The other is that this approach cuts the prostate during removal, which may pose a risk of tumor seeding (Bott et al., 2003).

Potential side effects or complications associated with a radical prostatectomy include temporary urinary incontinence and impotence. Urinary dysfunction subsides within the first year after surgery and potency is regained for approximately 80% of the patients (Bott et al., 2003). The return of these physical functions are dependent upon the patient’s age, the stage of the disease, and if nerve bundles are intact postoperatively. Many men who do not regain potency can benefit from oral medications, phosphodiesterase type 5 inhibitors, such as sildenafil (Bott et al., 2003). Sildenafil has the best results for patients less than 60 years of age who had a bilateral nerve-sparing procedure and had some spontaneous return of erectile function after surgery (Briganti et al., 2007). The effect of sildenafil improves over time, generally requiring between 12 to 24 months following surgery, and results indicated that 35% to 75% of these patients regained potency after a nerve-sparing surgery, compared to 0 to 15% of those who underwent non-nerve-sparing surgery (Briganti et al., 2007).

Robotic Prostatectomy

Robotic prostatectomy is a laparoscopic prostatectomy aided by a surgeon-assisted robot. This procedure increases visualization of delicate structures that surround the prostate, adds dexterity to the surgical removal, and eliminates surgeon-dependent hand movements (El-Hakim & Tewari, 2004). Data on the effectiveness of robotic prostatectomy are reported to be comparable to open and laparoscopic prostatectomy in terms of efficacy and clinical outcomes (El-Hakim & Tewari, 2004). Based on results from a meta-analysis by El-Hakim and Tewari (2004), robotic prostatectomy appears to be slightly more efficient at reducing complications related to impotency, urinary incontinence, and recovery time (Starnes & Sims, 2006). Robotic prostatectomy is slightly more expensive than other surgical procedures and may not be available at all treatment centers.

External Beam Radiotherapy

External beam radiotherapy treatment (EBRT) has similar efficacy to surgery (Bott et al., 2003) with some differing complications. EBRT is usually performed every weekday for 4 to 6 weeks. This procedure affects normal tissue, resulting in temporary adverse effects that include diarrhea, tenesmus, proctitis, dysuria, frequency, and lethargy. Long-term effects of EBRT include impotence in 10% to 30% of men and chronic proctitis. The latter of these complications may lead to bleeding and fibrosis. Incontinence is not usually a side effect from this treatment and disturbances in stool frequency are reported among fewer than 20% of men (Bott et al., 2003).

Brachytherapy

Brachytherapy involves the insertion of a radioactive source directly into the prostate gland. This procedure provides a high dose of radiation delivered locally, which spares surrounding normal tissue. Brachytherapy may be performed using either iodine-125 seeds or iridium-192 rods. Iodine-125 seeds are permanently placed and recommended for patients with a life expectancy of at least 10 years, a Gleason score of 6 or less, a prostate volume of less than 50 milliliters, and no previous prostate surgery. Potential complications associated with this procedure include irritation to the urethra, which results in incontinence and impotence (Bott et al., 2003). Iridium-192 rods are placed temporarily and recommended for patients with PSA results greater than 10 or a Gleason score between 8 and 10. Along with iridium-192 rod placement, EBRT is delivered over 4 weeks. Potential complications associated with this procedure include incontinence and impotence (Bott et al., 2003). Radiation damage to the urethra can result in both irritating and obstructive urinary symptoms. These symptoms may last up to 60 days, which is the half-life of the iodine rods. Approximately 10% to 15% of men who undergo brachytherapy experience erectile dysfunction, and use of phosphodiesterase type 5 inhibitors may be helpful in regaining sexual function (Bott et al., 2003).

Hormonal Manipulation

Patients with a Gleason score of 8 to 10 can benefit from at least 2 years of adjuvant luteinizing hormone-releasing hormone agonist therapy following EBRT, according to a review by Bott and associates (2003). Significant increases have been documented in disease-specific survival and overall survival with a median followup of over 5 years (Bott et al., 2003). At this time, the use of adjuvant hormonal therapy in conjunction with standard treatments is being researched. The results at this time seem promising, but further research is needed to determine the long-term effects on bone density and endocrine metabolism. The disease-specific survival figures must also be known before an approach such as this can be considered standard.

Followup Care

Serum PSA is synthesized almost exclusively by the prostate gland, making it an excellent method to assess treatment response. The PSA level should be decreased after treatment, and be close to zero after surgery. Routine screening using the PSA should continue to occur after treatment. A rising or elevated PSA level may indicate either residual prostate
cancer or recurrence and should be further investigated (Naito, 2005). Radiographic and nuclear medicine examinations can aid in detecting recurrent prostate cancer. If present, additional treatment may be recommended.

**PATIENT AND FAMILY EDUCATION**

Education, knowledge, and understanding are critically important to making an informed decision with respect to treatment decision making (Lepore, Helgeson, Eton, & Schulz, 2003). Education should include accurate information, pathophysiology, grading and staging, treatment options, and potential short and long-term side and adverse effects (Held-Warmkessel, 2002). In 2004, Fagerlin and associates performed a critical review of existing patient education materials for localized prostate cancer. They concluded that few materials were available which provided assistance in making treatment decisions. Most of the documents reviewed failed to describe all treatment options, did not contain complete information with respect to potential adverse effects of treatment, and required a high school reading ability to comprehend.

The Internet provides Web-based sources for health information. Patients and their families should be encouraged to visit nationally recognized sites, which provide accurate information. According to Fagerlin and associates (2004), the five highest rated patient education Web sites are the American Cancer Society (www.cancer.org), AstraZeneca (www.prostateinfo.com), Memorial Sloan-Kettering Cancer Center (www.mskcc.org), Cancer Care, Inc. (www.cancercare.org), and University of Toronto (www.prostatecentre.ca). These sites may be used to provide education, guide treatment decision making, and assist those diagnosed with prostate cancer to cope with their disease and treatment.

**References**


