Treatment Outcomes and Quality-of-Life Issues for Patients Treated With Prostate Brachytherapy

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The increasing popularity of brachytherapy for treatment of early-stage prostate cancer requires oncology nurses to have a comprehensive knowledge of the disease, its treatment, and management of side effects. Because quality-of-life (QOL) issues have become an important consideration in treatment selection for many patients, oncology nurses must have a thorough understanding of these QOL issues and their management. Armed with knowledge about prostate brachytherapy and its effect on QOL, oncology nurses can offer accurate information and evidence-based symptom management techniques to patients undergoing brachytherapy for prostate cancer. Key Words: prostatic neoplasms, radioisotope brachytherapy, quality of life

Risk Stratification

No prospective randomized trials have offered a comparative analysis of the efficacy of treatment options. Therefore, risk stratification based on pretreatment PSA, clinical staging, and the Gleason score has been invaluable in comparing treatment outcomes.

PSA is a protein produced by the lining of the prostate. In normal, healthy men, a small amount of this protein (0–4 ng/ml) can be detected in the bloodstream. In men with prostate cancer, a larger amount is produced. PSA also can be abnormally elevated in men with benign prostatic hypertrophy. However, in men diagnosed with prostate adenocarcinoma, the higher the pretreatment PSA (i.e., PSA level at the time of biopsy), the more likelihood exists for increased incidence of extracapsular extension, positive lymph node involvement, and positive margins (Partin et al., 1997).

The Gleason score is used to grade the aggressiveness of prostate cancer. This universally recognized scoring system is reliable, reproducible, time efficient, and of significant

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prognostic value (Steinberg, Sauvageot, Piantadosi, & Epstein, 1997). When evaluating a biopsy specimen, a pathologist assigns a primary Gleason grade of 1–5, which is added to a secondary Gleason grade of 1–5. The sum of the two numbers is the Gleason score. Gleason scores are separated into four groups based on the degree of differentiation: Gleason score of 2–4, 5–6, 7, and 8–10. In general, a low Gleason score represents a well-differentiated tumor and a high score reflects a poorly differentiated tumor. Sixty percent of all prostate adenocarcinomas have a Gleason score of 6–7 (Iczkowski & Bostwick, 1998). The higher the Gleason score, the more aggressive the disease and the poorer the prognosis.

Clinical staging, using the TNM classification system (T = primary tumor, N = regional lymph node involvement, and M = distant metastasis), is a universally recognized system used to characterize the extent of disease. Low-risk disease is defined as clinical T1 or T2a disease (T1 is a clinically inapparent tumor not palpable or visible by imaging, and T2a is a tumor confined to one lobe within the prostate gland) with a pretreatment PSA less than or equal to 10 ng/ml and a Gleason score lower than or equal to 6. Intermediate-risk patients present with one unfavorable parameter: a clinical stage higher than T2b, which refers to a tumor involving both lobes of the prostate; PSA greater than or equal to 10 ng/ml; or a Gleason score of 7 or higher. High-risk patients present with two or more unfavorable parameters: a clinical stage of T2b or T3a (extracapsular extension of disease), PSA greater than or equal to 10, or a Gleason score of 7 or higher (Merrick, Butler, Galbreath, & Lief, 2001).

Treatment Outcomes

By classifying patients according to pretreatment PSA, Gleason score, and clinical stage, clinicians are able to group patients and compare treatment outcomes. Outcomes are reported based on PSA progression after treatment for prostate cancer. Before PSA testing was available, men often were considered cured of prostate cancer if residual cancer was undetectable by digital rectal examination. Treatment results now are reported based on PSA progression after intervention. “The cure rate is estimated as the percentage of men without a rising PSA after several years post-treatment” (Wallner, 2000, p. 5.3). This often is referred to as biochemical no evidence of disease (bNED).

Patients with low-risk disease have excellent biochemical outcomes (as evidenced by freedom from PSA progression) after brachytherapy, external beam radiotherapy, or radical prostatectomy. In low-risk patients, brachytherapy as monotherapy has outstanding cure rates of 88%–96%, showing that supplementing their treatment with external beam radiotherapy would have no advantage (Blasko et al., 2000; Critz et al., 2000; Merrick et al., 2001b). In 1995, Blasko, Wallner, Grimm, and Ragde reported a five-year biochemical freedom from progression rate of 93%; in 2000, Blasko and colleagues reported nine-year bNED rates of 90%.

Most studies indicate that patients with intermediate- and high-risk disease have improved outcomes when treated with permanent prostate brachytherapy, whether or not supplemental external beam radiotherapy is used (Merrick, Butler, Lief, & Dorsey, 2001). This may be because of the ability of brachytherapy to deliver higher doses within the prostate gland and the periprostatic region, as patients with intermediate- and high-risk disease possess at least a 50% chance of extracapsular extension (Partin et al., 1997). For patients with intermediate-risk disease treated with brachytherapy alone, Blasko and colleagues (2000) reported a nine-year freedom from PSA progression rate of 82%. In the same study, no improvement in biochemical outcome was noted when external beam radiotherapy was added. Merrick, Butler, Galbreath, et al. (2001) reported a 97% six-year freedom from biochemical progression in hormone-naive patients with intermediate-risk disease who were treated with prostate brachytherapy, with or without supplemental external beam radiotherapy.

For patients with high-risk disease, 76%–80% five- to six-year biochemical disease-free survival rates have been reported for patients receiving external beam radiotherapy followed by prostate brachytherapy (Dattoli et al., 1999; Merrick, Butler, Lief, Galbreath, & Adamovich, in press). Figure 1 illustrates updated biochemical outcomes of hormone-naive, low-, intermediate-, and high-risk brachytherapy patients.

Patients with high-risk features often receive hormonal manipulation (i.e., administration of antiandrogens) in conjunction with prostate brachytherapy, despite a lack of evidence of improvement in biochemical outcomes. Three studies have demonstrated a possible benefit of hormonal manipulation (Lee, Stock, & Stone, 2002; Stone & Stock, 1999; Sylvester et al., 1999), but longer follow-up is needed. A retrospective, matched-pair analysis of 620 patients showed no benefit of hormonal manipulation when Gleason score, pretreatment PSA, or clinical stage were compared (Potters, Torre, Ashley, & Leibel, 2000). Two studies reported no improvement in biochemical outcome after hormonal manipulation for intermediate-risk patients or patients with Gleason scores of 5–9. However, patients with high-risk disease did demonstrate improved biochemical outcomes from hormonal manipulation (Merrick et al., 2001b; Merrick, Wallner, & Butler, in press). As such, hormonal manipulation remains controversial, requiring prospective, randomized trials to determine its efficacy.

Assessing Function

Accurate assessment of preimplant urinary, bowel, and sexual function is necessary for patients with prostate cancer. This baseline information should be obtained through patient-completed QOL instruments, which also may serve as reliable references in evaluating postimplant morbidities.

Schiller Cancer Center at Wheeling Medical Park in West Virginia uses several instruments to assess baseline urinary, bowel, and sexual function. The International Prostate Symptom Score (I-PSS) questionnaire assesses urinary function (see Figure 2), the Rectal Function Assessment Study (R-FAS) questionnaire evaluates bowel function (see Figure 3), and the International Index of Erectile Function (IIEF) questionnaire addresses sexual function (see Figure 4) (Barry et al., 1992; Merrick Butler, Dorsey, et al., 2000; Rosen et al., 1997). The three questionnaires are easily administered, practical, and reliable indicators of these QOL issues. To assess baseline status, the questionnaires can be given to patients to complete at the time of their first visit. Once nurses develop a rapport with patients, follow-up telephone interviews and mailed surveys can be conducted.
1. Over the last month or so, how often have you had a sensation of not emptying your bladder completely after you finished urinating?

0 = Not at all
1 = Less than one time in five
2 = Less than half the time
3 = About half the time
4 = More than half the time
5 = Almost always

2. During the last month or so, how often have you had to urinate again less than two hours after you finished urinating?

0 = Not at all
1 = Less than one time in five
2 = Less than half the time
3 = About half the time
4 = More than half the time
5 = Almost always

3. During the last month or so, how often have you stopped and started again several times when you urinated?

0 = Not at all
1 = Less than one time in five
2 = Less than half the time
3 = About half the time
4 = More than half the time
5 = Almost always

4. During the last month or so, how often have you found it difficult to postpone urination?

0 = Not at all
1 = Less than one time in five
2 = Less than half the time
3 = About half the time
4 = More than half the time
5 = Almost always

5. During the last month or so, how often have you had a weak urinary stream?

0 = Not at all
1 = Less than one time in five
2 = Less than half the time
3 = About half the time
4 = More than half the time
5 = Almost always

6. During the last month or so, how often have you had to push or strain to begin urination?

0 = Not at all
1 = Less than one time in five
2 = Less than half the time
3 = About half the time
4 = More than half the time
5 = Almost always

7. During the last month, how many times did you typically get up to urinate from the time you went to bed until the time you got up in the morning?

0 = None
1 = One time
2 = Two times
3 = Three times
4 = Four times
5 = Five or more times

8. How would you feel if you had to live with your urinary condition the way it is now, no better, no worse, for the rest of your life?

0 = Delighted
1 = Pleased
2 = Mostly satisfied
3 = Mixed
4 = Mostly dissatisfied
5 = Unhappy
6 = Terrible

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**Figure 2. Questions From the Symptom Index for Benign Prostatic Hyperplasia**

1. Frequency of stools per day
   - 0–1 stool per day
   - 2 stools per day
   - 3 stools per day
   - 4 or more stools per day
2. Consistency of stools
   - All stools formed
   - Stools formed and loose
   - Stools loose
   - Watery stool
3. Urgency of stools
   - No urgency
   - Somewhat urgent
   - Urgent
   - Very urgent
4. Abdominal discomfort
   - No discomfort
   - Mild to moderate discomfort
   - Somewhat severe discomfort
   - Very severe discomfort
5. Hemorrhoidal discomfort
   - No discomfort
   - Requires mild treatment (i.e., tucks, sitz baths)
   - Requires topical medication (e.g., Preparation H® [Wyeth Consumer Healthcare, Madison, NJ])
   - Requires oral analgesics or narcotics for relief
6. Rectal bleeding
   - No rectal bleeding
   - Blood on toilet paper one time per week
   - Blood on toilet paper two to three times per week
   - Blood on toilet paper more than four times per week
7. Continence
   - Normal continence; able to control stool movements at all times
   - Gas incontinence only; able to control stool movements but not gas
   - Minor spotting or leakage of stool (up to coin size) more than once per week
   - Significant leakage of stool (larger than coin size) about once per week
   - Significant leakage of stool (larger than coin size) more than once per week
8. Nighttime bowel movement (total number of nights in last week that you had to get up from bed to have a bowel movement)
   - 0
   - 1
   - 2
   - 3
   - 4
   - More than 5
9. Completeness of evacuation
   - Complete evacuation (requires one movement to completely empty bowel or feel you are “all done”)
   - Occasional multiple evacuations (about once a week; feel like you are not “all done” or it takes more than one movement to finish)
   - Frequent multiple evacuations (more than once a week; feel like you are not “all done” or it takes more than one movement to finish)
   - Requires enema to obtain complete emptying

**Figure 3. Questions From the Rectal Function Assessment Study**

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North Chicago, IL), and doxazosin mesylate (Cardura®, Pfizer Pharmaceuticals, New York, NY). Tamsulosin hydrochloride often is the drug of choice because it does not evoke the hypertensive response often encountered with terazocin hydrochloride or doxazosin mesylate. Treatment with either of the latter two drugs necessitates that patients’ blood pressure be monitored and documented on a regular basis, such as daily for one week, then weekly until it stabilizes. Patients must be educated to watch for and report episodes of vertigo, lightheadedness, or syncope. Serial telephone conversations and mailed QOL surveys using the I-PSS score also allow nurses to assess urinary function, patients’ responses, and comfort levels in an ongoing fashion, allowing alpha-1 blocker therapy to be adjusted appropriately (Abel et al., 2000).

Dysuria, perhaps the most common complaint postoperatively, varies from minimal irritation to extreme burning. When patients experience dysuria, urinalysis and urine cultures must be obtained to rule out urinary tract infection. Urinary tract infections are common after implantation because many patients do not empty their bladders completely with each void. In the absence of infection, dysuria often responds well to treatment with ibuprofen (400 mg orally three times daily with meals). The anti-inflammatory properties of ibuprofen decrease urethral and prostate edema. If dysuria persists, phenazopyridine (Pyridium®, Warner-Chilcott Laboratories, Rockaway, NJ) (200 mg orally three times daily) may be prescribed. Increased oral liquid intake helps keep the urine dilute and may diminish symptoms further. Patients also should be encouraged to avoid intake of caffeinated and alcoholic beverages, well-known bladder irritants.

Hematuria usually is minimal and transient, resolving within the first three days postimplant. Postoperatively, patients should be encouraged to drink at least eight ounces of noncaffeinated fluids every hour until the urine is clear to help flush the bladder of clots, which can cause urinary obstruction. Patients should not be discharged until they have voided three times, at least 100 cc per void. Urine should be clear to pink-tinted and clot-free prior to discharge. Ultrasound of the bladder can be used to determine whether patients are emptying their bladders adequately. On rare occasions, patients must remain in the hospital overnight for continuous bladder irrigation because of hematuria.

Late urinary effects of brachytherapy can include urethral strictures. The incidence of development of a urethral stricture five years postimplant has been reported at 5%–12% and always involves the membranous urethra (Merrick et al., 2001a; Ragde et al., 1997). Strictures have been well managed by dilatation. Computerized tomography-based dosimetric evaluations confirmed that doses to the bulbomembranous urethra were significantly higher in patients who developed strictures than those who did not (Merrick et al., 2001a). Improvements in brachytherapy techniques have resulted in more accurate seed placement, confining the radiation dose to the target area with a steep dose gradient beyond it (Merrick, Butler, Lief, et al., 2001). With improved techniques, the radiation dose to the bulbomembranous urethra is decreased, resulting in an expected downward trend in the development of urethral strictures.

Urinary incontinence is rare after prostate brachytherapy, occurring in less than 1% of the patient population, unless a prior transurethral resection was performed (Blasko, Grimm, & Ragde, 1993; Merrick et al.,...
1. How often are you able to get an erection during sexual activity?
0 = No sexual activity
1 = Almost never/never
2 = A few times (much less than half the time)
3 = Sometimes (about half the time)
4 = Most times (much more than half the time)
5 = Almost always/always

2. When you had erections with sexual stimulation, how often were your erections hard enough for penetration?
0 = No sexual activity
1 = Almost never/never
2 = A few times (much less than half the time)
3 = Sometimes (about half the time)
4 = Most times (much more than half the time)
5 = Almost always/always

3. When you attempted sexual intercourse, how often were you able to penetrate (enter) your partner?
0 = Did not attempt intercourse
1 = Almost never/never
2 = A few times (much less than half the time)
3 = Sometimes (about half the time)
4 = Most times (much more than half the time)
5 = Almost always/always

4. During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?
0 = Did not attempt intercourse
1 = Almost never/never
2 = A few times (much less than half the time)
3 = Sometimes (about half the time)
4 = Most times (much more than half the time)
5 = Almost always/always

5. During sexual intercourse, how difficult was it to maintain your erection to completion?
0 = Did not attempt intercourse
1 = Extremely difficult
2 = Very difficult
3 = Difficult
4 = Slightly difficult
5 = Not difficult

6. How do you rate your confidence that you could get and keep an erection?
1 = Very low
2 = Low
3 = Moderate
4 = High
5 = Very high

7. How often have you experienced pain at the time of orgasm?
0 = No sexual activity
1 = Almost never/never
2 = A few times (much less than half the time)
3 = Sometimes (about half the time)
4 = Most times (much more than half the time)
5 = Almost always/always

8. How often have you noted blood in the ejaculate?
0 = No sexual activity
1 = Almost never/never
2 = A few times (much less than half the time)
3 = Sometimes (about half the time)
4 = Most times (much more than half the time)
5 = Almost always/always

9. Have you noted a change in the intensity of your orgasm?
☑ Yes
☐ No

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**Figure 4. Questions From the International Index of Erectile Function**

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2001a). With prior transurethral resection, the incidence of urinary incontinence is reported to be 12.5% (Ragde et al., 1997). When peripheral-based seed distributions were used and the urethral dose was limited, urinary stress incontinence was reported in only 6% of patients who underwent transurethral resection of the prostate (Wallner, Lee, Wasserman, & Dattoli, 1997).

**Rectal Morbidity**

Following prostate brachytherapy, less than 5% of patients develop radiation-induced proctitis, or inflammation of the rectum or anus (Blasko et al., 1993; Wallner et al., 1996). Mild rectal irritation or bowel frequency occurs rarely in the first couple of weeks after surgery. Long-term bowel dysfunction is relatively uncommon, as reported by patients on completed questionnaires (i.e., R-FAS) (Merrick et al., 2001a). Late-onset proctitis typically occurs between the first and second year postimplant, characterized by intermittent rectal bleeding. More severe complications, such as rectal ulceration and fistula formation, are exceedingly rare (Howard, Wallner, & Han, in press).

Proctitis usually is self-limited and managed easily with topical or suppository applications of cortisone preparations and the use of sitz baths to alleviate rectal discomfort. If rectal bleeding is significant or if it persists, colonoscopic evaluation is recommended to rule out other pathology. Patients should consult with their physicians before consenting to biopsy of their rectums or lower colons, as radiation changes in the tissues may render patients more susceptible to ulceration or fistula formation. If rectal bleeding persists and does not respond to traditional therapies, instillation of 4% formalin solution into the rectum is a safe and effective outpatient treatment for radiation-induced hemorrhagic proctitis, with cessation of bleeding noted in 90% of cases (Froese, 2001).

A recent case study of interest noted that acute or chronic constipation postoperatively might significantly increase the radiation dose to the rectum (Merrick, Butler, Dorsey, & Dorsey, 2000). Although previous studies have not found a correlation among prostate size, dose to the rectum, and rectal complications, rectal distension associated with constipation may increase the radiation dose to the rectum (Stone & Stock, 2000; Wallner et al., 1996). To avoid rectal distension, bulking agents may be helpful in regulating bowel habits postoperatively.

**Erectile Dysfunction**

Erectile dysfunction (ED) affects as many as 30 million American men. It can be the result of the natural aging process and is a common sequela of all potentially curative treatment modalities for prostate cancer (National Institutes of Health [NIH] Consensus Development Panel on Impotence, 1993). ED
occurs as a result of local trauma, neurogenic impairment, vascular compromise, and psychogenic factors (Zelesky & Eid, 1998). The NIH Consensus Development Panel defined ED as “the inability to attain or maintain a penile erection sufficient for satisfactory sexual performance” (p. 83).

ED occurs in 6%–61% of cases after prostate brachytherapy, with or without supplemental external beam radiotherapy (Merrick et al., 2001a). The wide range may be because of differences in definition, as well as variation in the mode of data collection and length of follow-up. Differences in the patient population studied also may account for statistical discrepancies. For example, if an elderly population is evaluated, ED will be more prevalent simply as a result of the natural aging process.

Potency after prostate brachytherapy should be assessed via a patient-administered questionnaire. One study suggested that physicians tend to underestimate the incidence of ED because it is highly subjective (Litwin, Lubeck, Henning, & Carroll, 1998). For this reason, direct patient survey is the preferred means of assessment. Pretreatment erectile function is the strongest predictor of ED (Merrick et al., 2002; Stock, Kao, & Stone, 2001). Therefore, using the specific erectile questions of the IIEF has proven invaluable in anticipating outcomes and assessing the effectiveness of therapeutic interventions (Stipetich et al., 2002). Diabetes mellitus and the use of supplemental external beam radiation also are associated with the development of post-treatment ED. Merrick and colleagues (2002) reported an overall six-year actuarial incidence of potency preservation at 39% after brachytherapy. However, 52% of patients not receiving supplemental external beam radiation maintained potency. Fortunately, most men experiencing brachytherapy-induced ED respond well to sildenafil citrate (Viagra®, Pfizer Pharmaceuticals). In men who were fully potent prior to treatment but impotent after implantation, 95% responded favorably to sildenafil citrate. Those who reported suboptimal preimplant erectile function responded in 70% of cases (Merrick et al., 2002).

Nurses must counsel patients prior to treatment about sildenafil citrate. Sildenafil citrate 50 mg may be taken one hour prior to intercourse, with the effects lasting as long as four hours. The dose can be doubled to 100 mg if three attempts at 50 mg are unsuccessful. It is generally well tolerated with rare side effects, such as nausea, headache, and facial flushing. Even more uncommon are reports of visual changes, such as colors appearing tinged, increased sensitivity to light, and blurred vision. Sildenafil citrate is contraindicated in patients with a cardiac history on nitrate therapy. Rare reports of life-threatening hypertensive episodes and deaths have been reported in these patients (PDR, 2002; Pfizer Pharmaceuticals, 2001).

Several other options are available to treat ED. Prostaglandin E tablets inserted into the urethra enhance penile blood flow, with improvement in erectile function in 20% of men (Wallner, 2000). In men who have some natural erectile function, a penile ring can be placed on the base of the penis after achieving as much of an erection as possible, preventing the outflow of blood from the penis. An electronic or hand-operated vacuum pump can be used to develop an erection by placing it around the penis to draw blood into the penis, with the placement of a penile ring at the base of the penis to preserve the erection. More than 60% of men have found success with injection of drugs (i.e., papaverine, phentolamine, or prostaglandins) directly into the base of the penis, causing vasodilatation with subsequent erection (Wallner). Although they are not considered painful, repeated injections may cause some minor scarring over time.

The final method that can be used to restore erectile ability is surgical insertion of a permanent plastic device into the penis. The device can be a semiflexible rod that can be bent into position as needed or a manually inflated pump that can be inserted at the base of the penis or in the scrotum, which then inflates the penis when the fluid-filled reservoir is pushed. Although the implanted devices are very effective, complications are more likely. Infection or mechanical difficulties may necessitate the removal of such a device, resulting in scarring or shortening of the penis. Fortunately, many options exist for the treatment of ED, but the method selected should be individualized to each patient, with great care taken to maintain confidentiality.

Conclusion

Treatment of prostate cancer with prostate brachytherapy is an ever-evolving science. With continued improvements in implantation techniques, morbidity from treatment will decrease and high biochemical disease-free survival rates will continue. As more and more patients make treatment decisions based on QOL issues, keeping abreast of ongoing research and advances is essential for oncology nurses. Continued research and prospective studies will enable healthcare professionals to lessen treatment morbidity while improving comfort levels.

References


Rapid Recap

**Treatment Outcomes and Quality-of-Life Issues for Patients Treated With Prostate Brachytherapy**

- Refinements in prostate brachytherapy techniques have significantly improved the accuracy of seed placement.
- Quality-of-life issues such as urinary morbidity, rectal morbidity, and erectile dysfunction affect decisions about treatment.
- The most common side effects of prostate brachytherapy include urinary irritative symptoms, self-limited proctitis, and impotence.
- Self-administered questionnaires help researchers identify the onset, severity, and duration of urinary, bowel, and sexual dysfunction that may occur as a result of prostate brachytherapy treatment.
- Stratifying patients into groups based on pretreatment prostate-specific antigen tests, Gleason score, and clinical stage allows comparison of treatment outcomes.
- Prostate brachytherapy is used to treat low-risk, intermediate-risk, and high-risk prostate cancer, with favorable results and decreased incidence of urinary and rectal morbidity and acceptable rates of sexual dysfunction.