Erectile dysfunction is a well-known complication of all treatments for prostate cancer. Following nerve-sparing radical prostatectomy (RP), the impotence rate at academic centers has been shown to be as high as 32% to 38%\(^1,2\) and is even greater (60% to 70%) in community-based surgical series.\(^3,4\) Likewise, there is a significant incidence of erectile dysfunction (ED) following external beam radiotherapy and interstitial brachytherapy when patients are followed for at least 2 years after treatment (23% to 56% and 27% to 53%, respectively).\(^5-8\)

There is little doubt that patients consider the risk of ED when choosing treatment for prostate cancer. In fact, patients value sexual function so highly that they are often willing to choose a therapy that offers a shorter life expectancy but better potency following treatment. Hemigason and colleagues interviewed 299 healthy men aged 50 to 80 and specifically asked subjects to imagine that they had localized prostate cancer. They were then asked if they would be willing to undergo a cancer treatment that could possibly lengthen life expectancy but cause loss of current sexual function. Nineteen percent of subjects were unwilling to accept treatment regardless of life expectancy benefit, while an additional 28% would accept the treatment only if it resulted in an improvement of more than 10 years in life expectancy over no treatment.
Patients strongly consider quality, as well as quantity, of life when choosing a treatment for prostate cancer.

In a another study, Singer and colleagues presented a series of 50 healthy men aged 45 to 70 with a similar hypothetical situation. In this study, patients were told that they could choose between “treatment A,” which would result in excellent five-year survival but also impotency, or “treatment B,” which would allow them to maintain their sexual function but would result in a reduction of at least 10% in 5-year survival. Although 32% of subjects chose “treatment A,” indicating that they were unwilling to trade a 10% or greater risk of at least 10% in 5-year survival, the importance of understanding quality of life following treatment for localized prostate cancer becomes even greater.

Advances in research methodology now allow reliable collection of meaningful data regarding patients’ health-related quality of life (HRQOL). HRQOL includes both objective evaluation of patients’ functional status and their perceptions of their own health and its impact on their existence. In the past decade, several validated and reliable questionnaires have been developed that are specifically designed to measure HRQOL in men with prostate cancer. These surveys have been used to compare the effects of various treatments on quality of life, allowing us to reach meaningful conclusions that may be helpful in assisting patients when choosing therapy for their disease. The impact of quality of life on therapeutic decision-making is now considered so important that some investigators have suggested that a clinical cancer trial is incomplete without assessment of HRQOL as a measure of outcome. This article will focus primarily on the effect of sexual dysfunction on quality of life following treatment for localized prostate cancer.

The Measurement of Health-Related Quality of Life

In order to understand the effect of ED on quality of life in men with prostate cancer, one must be familiar with how HRQOL is measured. Many physicians mistakenly believe that they can reliably determine a patient’s current quality of life during the clinical visit. In a study of 2,252 men with prostate cancer and their doctors, researchers compared patients’ self-assessments of HRQOL with physicians’ estimates of the patients’ quality of life. Of the patients, 74.5% reported fatigue, while only 10% of their physicians believed that the patient experienced this symptom. Furthermore, 97% of patients reported some degree of sexual dysfunction, while only 52.4% of their physicians reported that the patient had this problem. This study underscores the importance of collecting quality-of-life information directly from the patient. HRQOL is, therefore, measured by directly questioning the patient using surveys (also known as instruments). These questionnaires can be administered in a standardized fashion by an objective third-party interviewer, or they can be self-administered by the patient. The instruments are developed using the principles of psychometric test theory and are rigorously tested and reviewed prior to use to insure that collected data are both valid and reliable.

HRQOL instruments typically contain questions (also known as items) that are organized into scales. Each scale measures a different aspect, or domain, of HRQOL. For example, items inquiring about libido, erectile function, and orgasm might be grouped together into a scale measuring the sexual domain of HRQOL. Domains can be either general or disease-specific. General domains address the aspects of HRQOL that are common to all patients regardless of their disease process. Examples of general HRQOL domains include general physical, emotional, or social functioning, general health perceptions, and overall vitality. Disease-specific domains focus on the impact of particular organic dysfunctions associated with the disease that may affect HRQOL. Prostate-cancer specific domains include nausea, bony pain, anxiety regarding cancer recurrence, urinary or sexual dysfunction, and so forth.

Given the unique influence of sexual function on an individual’s sense of self, there are a number of caveats that should be followed when assessing the effect of ED on HRQOL. First, quality-of-life assessments should be targeted to the patient’s current or very recent HRQOL status. In other words, studies that query that patient about his sexual function 6 to 12 months before treatment may produce questionable results, as patients tend to exaggerate their potency.
illustrate this point, Litwin and McGuigan\(^\text{13}\) assessed HRQOL in 107 men immediately prior to RP. At an average of 21 months following surgery, they asked the same patients to recall their preoperative quality of life. They found that patients overestimated their baseline HRQOL in the urinary and sexual function domains by 13% and 27%, respectively. This underscores the need to collect HRQOL in a prospective, longitudinal setting whenever possible.

Furthermore, it is important to collect both “function” and “bother” information when assessing the effect of ED on quality of life. “Function” refers to the degree of symptoms that a patient experiences. If one questions a patient regarding the symptoms that a patient experiences. If one questions a patient regarding the degree of problems that he has experienced due to his sexual dysfunction, bother is being measured. Gill and Feinstein\(^\text{14}\) performed an extensive review of the literature and determined that the vast majority of HRQOL instruments assess only function. While this may be adequate in certain medical conditions, it is particularly problematic when assessing the effect of ED on quality of life, as function and bother do not necessarily correlate,\(^\text{15}\) as will be demonstrated below.

**HRQOL Instruments in Prostate Cancer**

Many providers use the International Index of Erectile Function (IIEF)\(^\text{16}\) to assess potency after treatment for prostate cancer. While this instrument is clinically useful as a functional scale to measure severity of ED, it is not a true measure of HRQOL. The three most commonly used HRQOL instruments for prostate cancer are:

- **UCLA prostate cancer index.** The UCLA PCI was the first validated instrument specifically designed to measure HRQOL in prostate cancer patients.\(^\text{15,17}\) It is a 56-item, self-administered survey that takes about 20 minutes to complete. The first 36 items measure general HRQOL, while the remaining 20 items are prostate-specific and are scored in 6 scales (urinary function and bother, sexual function and bother, and bowel function and bother) from 0 to 100, with higher scores representing better outcomes. The UCLA PCI is now in use in many national and international studies, and has recently been validated in Spanish.\(^\text{18}\)

The UCLA PCI is the only HRQOL instrument for prostate cancer that makes the important distinction between function and bother in the prostate-specific domains. By assessing bother, the UCLA PCI goes beyond simply measuring functional status and attempts to quantify the degree to which a patient’s symptoms actually interfere with his quality of life. Because the urinary domains of the UCLA PCI are primarily focused on the impact of incontinence of HRQOL, Wei and colleagues\(^\text{19}\) recently developed a modified version of the instrument, called the Expanded Prostate Cancer Index (EPIC), which also addresses the impact of irritative voiding symptoms and hormone ablation therapy on HRQOL. Although the EPIC instrument may represent an improvement, the UCLA PCI is still generally considered the “gold standard” for HRQOL research in men with localized disease.

The EORTC core quality of life questionnaire. The EORTC QLQ-C30 was originally designed to measure cancer-specific HRQOL in patients with different types of malignancies, including prostate, lung, head and neck, breast, and ovarian malignancies.\(^\text{20}\) The first 30 items of the instrument address the various domains that are common to all cancer patients. The 20 items of the prostate cancer module instrument comprise a bowel symptom scale, urinary symptom scale, and sexuality scale, and has been shown to be valid and reliable in men with both localized\(^\text{21,22}\) and metastatic\(^\text{23}\) prostate cancer. Unlike the UCLA PCI, neither the EORTC QLQ-C30 nor its prostate cancer-specific module distinguishes between function and bother in its domain. The EORTC QLQ-C30, however, may be better suited than the UCLA PCI to measuring HRQOL in patients with advanced disease, given its unique symptom scales.

The functional assessment of cancer therapy-prostate instrument. Like the EORTC QLQ-C30, the FACT was originally developed for use in patients with all types of cancer.\(^\text{24,25}\) The general instrument (or FACT-G) contains 28 items and is self-administered. Esper and colleagues\(^\text{26}\) developed the FACT-P, which incorporated a 12-item subscale that includes items concerning weight loss, appetite, urination difficulties, and erectile dysfunction. The 12 items were then used to create a single summary score for problems caused by prostate cancer. Although the FACT-P addresses the important quality-of-life issues faced by prostate cancer patients, the use of single items and the creation of a single summary score...
may not be optimal. Once again, no distinctions are made between function and bother.

Sexual Dysfunction and Quality of Life Following Radical Prostatectomy
Radical retropubic prostatectomy is the most common surgical treatment for localized prostate cancer. As mentioned earlier, this procedure is associated with a significant incidence of postoperative sexual dysfunction. A recent publication from the Prostate Cancer Outcomes Study\(^4\) reported longitudinal quality-of-life outcomes in a population-based cohort of 1291 men who underwent RP for localized disease. They used the Surveillance, Epidemiology, and End Results (SEER) cancer registries to accrue patients diagnosed with localized prostate cancer from October 1, 1994, through October 31, 1995, in six geographic regions. At baseline, 73% of men reported erections firm enough for intercourse, and 45% of men reported no difficulty in maintaining an erection. An important finding was that when questioned as to how big a problem their sexual function was at 2 years following surgery, 14% said it was no problem, 23% said it was a small problem, and 42% said it was a moderate to big problem. Although this study suffers from significant missing data (at 2 years, 21% of patients did not report whether or not they were having erections firm enough for intercourse) and also used a questionable technique for assessing preoperative sexual function, it still demonstrates a number of valid and important points. First, patients have a significant amount of sexual dysfunction following surgery. Secondly, this dysfunction impacts quality of life, as a considerable number of patients experience bother from their symptoms. Finally, the degree of function and bother do not correlate as well one might expect, indicating that the effect of ED on patients’ quality of life is variable and highly individualized.

Other authors have also examined the relationship between sexual function and bother following RP. Bates and colleagues\(^27\) assessed HRQOL using the ICS-male questionnaire in 83 men who underwent radical retropubic prostatectomy. Of the 74 men who reported preoperative potency, 44 (59%) were completely impotent. However, 45% of these impotent men reported that this was not a problem, and 20% reported that it was only a “bit of a problem.” This finding is not limited to the postprostatectomy setting. In a study of 528 men, including 214 men with localized prostate cancer who underwent surgery, radiotherapy, or watchful waiting, and 273 controls, level of sexual function was compared to degree of bother experienced. Although there was a reasonable correlation (90% of men with good or very good sexual function experienced no or very little bother, while 78% with poor or very poor sexual function experienced great bother from their condition), there was still a considerable number of patients in whom function and bother did not agree (see Table 1). While these reports illustrate the negative effect of ED on quality of life, they underscore the need to approach each patient individually, as each patient experiences sexual dysfunction in a profoundly personal manner.

To explore the effect of the nerve-sparing RP technique on quality-of-life outcomes, Talcott and colleagues\(^28\) compared 28 men who underwent non-nerve-sparing RP to 66 men who underwent either unilateral or bilateral nerve-sparing surgery at a single institution. They found that men who underwent nerve-sparing surgery had significantly better sexual function at 6, 12, and 18 months following treatment than those who had non-nerve-sparing surgery.

<table>
<thead>
<tr>
<th>Level of Function</th>
<th>Degree of Bother</th>
<th>Moderate</th>
<th>Great</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good or very good</td>
<td>None, Very Small, or Small</td>
<td>102 (90%)</td>
<td>8 (7%)</td>
</tr>
<tr>
<td>Very poor or poor</td>
<td>None, Very Small, or Small</td>
<td>36 (12%)</td>
<td>30 (10%)</td>
</tr>
</tbody>
</table>

*Cohort of 214 men with localized prostate cancer and 273 age-matched controls.

Data from Litwin and colleagues.

Table 1
Relationship Between Level of Sexual Dysfunction and Degree of Sexual Bother*
The Effect of Erectile Dysfunction

The Effect of Erectile Dysfunction

statistically significant differences in sexual functioning between the nerve-sparing and non-nerve-sparing groups. Another study used a multicenter observational disease registry to compare longitudinal HRQOL in 218 men who underwent nerve-sparing RP to that in 124 men who underwent the non-nerve-sparing technique. They found that the patients who underwent nerve-sparing surgery had significantly better sexual function at 6, 12, and 18 months following treatment than those who had non-nerve-sparing surgery, although the overall level of sexual function was low for both groups. Given the multi-institutional nature of this study, these results probably better represent the effectiveness of nerve-sparing surgery in the general population.

Sexual Function and Quality of Life Following Radiotherapy

Sexual dysfunction can occur following both external beam radiotherapy (EBRT) and interstitial brachytherapy (IB), presumably due to radiation injury to the neurovascular bundles adjacent to the prostate. There are considerably more data on ED and quality of life in the setting of EBRT than for IB, as the current techniques of radioactive seed implantation have gained widespread acceptance only in the last 5 years.

Mantz and colleagues studied 287 men with localized prostate cancer who underwent conformal EBRT. They noted actuarial potency rates of 96%, 75%, 59%, and 53% at 1, 20, 40, and 60 months after therapy. However, similar to the situation following surgery, the effect of ED on quality of life is highly individualized. Reddy and colleagues noted that 79% of patients who were potent prior to radiotherapy reported that the treatment qualitatively reduced their ability to obtain an erection. Despite this, 91% of patients were satisfied with their treatment, demonstrating that sexual dysfunction and satisfaction with therapy do not correlate.

As with RP patients, sexual dysfunction appears to cause EBRT patients significant bother. In a cohort of 432 EBRT patients, 37% reported that their sexual function was a “medium or big problem.” Helgason and colleagues studied 53 men who had undergone EBRT for localized prostate cancer and noted that 77% reported diminished sexual desire, 34% reported erections insufficient for intercourse, and 77% of men reported some loss of stiffness. More important, 50% of men reported that their overall quality of life had decreased much or very much as a direct result of their decrease in erectile function. Other researchers have found that sexual dysfunction has less of an effect on quality of life following EBRT. Caffo and colleagues showed that although 44% of men had significant sexual dysfunction following EBRT, general quality of life, measured as physical, psychological, and relational well-being, remained good.

Preliminary data from patients undergoing IB indicate that this treatment also has an effect on sexual function and quality of life. Initial reports indicated that IB had minimal effect on sexual function. Arterbery and colleagues reported that 87% of 35 patients who were potent pretreatment maintained their potency 6 months following treatment. However, larger studies with longer follow-up have reported a higher incidence of sexual dysfunction. In a study directly comparing outcomes between men undergoing surgery and IB and age-matched controls, Brandeis and colleagues found that at 3 to 17 months following treatment, sexual function in the IB group was significantly worse than in age-matched controls. There were no significant differences between the RP and IB groups in either of the sexual domains. Other case series of men

Main Points

• Health-related quality of life assessment includes both objective evaluation of patients’ functional status and their perceptions of their own health and its impact on their existence.
• Assessment instruments contain questions organized into scales measuring different aspects, or “domains,” of HRQOL. Domains can be either general or disease-specific.
• “Function” measures the degree of symptoms that a patient experiences; “bother” measures the degree of problems the patient has experienced due to symptoms.
• Loss of sexual function may not be perceived by the patient as a problem.
• No statistically significant differences in sexual functioning were found among patients after nerve-sparing radical prostatectomy and after non-nerve-sparing surgery.
• Sildenafil appears to be effective in improving sexual function following treatment for localized prostate cancer.
undergoing IB have noted similar findings. As we gain greater experience and longer follow-up with men undergoing brachytherapy, the exact relationship between IB, ED, and quality of life will become clearer.

The Effect of Erectile Aids on Quality of Life in Men Who Have Undergone Treatment for Localized Prostate Cancer

Given the high incidence of ED following treatment for prostate cancer, one would suspect that a significant number of patients would use erectile aids. In the report discussed earlier from the Prostate Cancer Outcomes Study, 27% of men had used a vacuum erection device, 21% penile injections, and 9% oral medications, 8% had received counseling, and 4% had had a penile prosthesis. As data collection for this study occurred prior to the United States Food and Drug Administration’s approval of sildenafil, one would expect that although the distribution of treatments may have changed, the overall use of erectile aids would have increased.

Sildenafil appears to be effective in improving sexual function following treatment for localized prostate cancer. In the postsurgical patient, it appears that efficacy is directly related to whether or not nerve-sparing surgery was performed. When bilateral nerve-sparing is performed, 72% of patients who did not use erectile aids. Interestingly, when asked about their overall quality of life, however, no differences were noted between the groups. While this study demonstrates that the use of erectile aids improves disease-specific quality of life in patients who have undergone treatment for localized prostate cancer, it fails to show that the use of these aids improves the patient’s overall quality of life. Further research, focused on the effect of sildenafil on both disease-specific and general HRQOL, is needed to determine if treatment for erectile dysfunction improves quality of life in men treated for prostate cancer.

Conclusions

There is a significant incidence in sexual dysfunction following all treatments for localized prostate cancer. This appears to have a significant impact on patients’ quality of life regardless of the choice of initial treatment. This effect, however, seems to be variable, as some patients with significant sexual function experience little bother from their problem, while others may experience minimal dysfunction but significant bother. Providers need to be aware of the highly individualized nature of the relationship between ED and quality of life when discussing treatment options with their patients. Further research is important to determine if the use of erectile aids in general, and sildenafil in particular, improve quality of life in men with sexual dysfunction following treatment for localized prostate cancer.

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The Effect of Erectile Dysfunction


