

Chapter 2

The Impact of Prostate Cancer Diagnosis and Post-treatment Sexual Dysfunction on Quality of Life

David F. Penson and Christian J. Nelson

1	Assessing Quality of Life in Prostate Cancer Survivors	18
2	The Effect of Prostate Cancer Diagnosis on Generic Quality of Life	19
3	The Psychological Effect of a New Prostate Cancer Diagnosis	21
4	The Effect of Post-treatment Sexual Dysfunction on Quality of Life	23
4.1	Radical Prostatectomy	23
4.2	External Beam Radiotherapy	26
4.3	Interstitial Brachytherapy (Seeds)	27
5	The Psychological Effect of Post-treatment Sexual Dysfunction	27
6	Conclusions	28
	References	29

Abstract There is little doubt that prostate cancer is a significant public health burden. The malignancy continues to be the most common solid tumor among American men and the second leading cause of cancer death (1). However, not all prostate malignancies are deadly and, in fact, a significant number of newly detected prostate tumors are “overdiagnosed” (2). In other words, had the patient never been screened for prostate cancer, he never would have known he had the disease and, more importantly, he never would have suffered any clinical sequelae from the tumor. This observation, coupled with the fact that, to date, there are no adequately sized randomized clinical trials documenting that one active therapy is superior to another in terms of overall or disease-specific survival, has caused patients and providers to strongly consider quality of life when choosing therapy for prostate cancer. In fact, some studies have shown that survivors value quality of life to a much greater degree than the impact of treatment on survival when choosing therapy for localized prostate cancer (3). To this end, it is critical to understand both the effect of the diagnosis of prostate cancer on quality of life and also the impact of sexual dysfunction on quality of life in men with this disease. The goal of this chapter is to review the effect of prostate cancer diagnosis and post-treatment sexual dysfunction on quality of life.

Keywords Prostate cancer; sexual dysfunction; quality of life.

1 Assessing Quality of Life in Prostate Cancer Survivors

In order to assess the effect of prostate cancer and sexual dysfunction on quality of life, we must be able to measure this rather nebulous entity. To aid in this endeavor, we use a variable from the field of health services research, 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 (4). It should be noted that these surveys usually measure different aspects, or domains, of HRQOL, thus providing a more comprehensive portrait of the survivorship experience. For the most part, these domains can be broken into two categories: generic and disease-specific. Generic domains address the aspects of HRQOL that are common to all patients, regardless of their disease process. Examples of generic 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, etc. In this chapter, we will focus almost exclusively on the sexual domains.

Many physicians mistakenly believe that they can accurately assess a patient's quality of life from the clinical interaction. Studies have shown, however, that this is not the case. In a study from CaPSURE, a longitudinal observational disease registry of men with prostate cancer, patient-reported health-related quality of life in 2,252 prostate cancer survivors was compared to physicians' estimates of the patients' quality of life. Seventy-five percent of patients 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% of their physicians reported that the patient had this problem (5). 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. 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 effect 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.

Given the unique effect of sexual function on a man's gender identity and sense of self, there are two key points that must be considered when assessing the relationship of sexual dysfunction and HRQOL in prostate cancer. Firstly, it is probably important that HRQOL assessments be targeted to the patient's current or very recent sexual function status. In other words, studies that query the patient

about his pre-treatment sexual function 6–12 months earlier may produce questionable results, as patients tend to exaggerate their earlier potency. To illustrate this point, Litwin and McGuigan (6) 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 pre-operative quality of life. They found that patients overestimated their baseline HRQOL in the urinary and sexual function domains by 13 and 27%, respectively. In contrast to this, Legler and colleagues (7) compared responses to a pre-treatment HRQOL survey in 133 men in the Prostate Cancer Outcomes Study (PCOS) to recall function in these same patients 6 months later. Specifically in the sexual function domain, the correlation coefficient comparing pre-treatment scores to 6-month scores was 0.69, indicating reasonable agreement between the two scores. In summary, while there may be less recall bias than one might think, it is always better to collect HRQOL information in a prospective, longitudinal setting whenever possible.

The second unique consideration when assessing the effect of sexual dysfunction on HRQOL is the importance of collecting both function and bother information. Function refers to the degree of symptoms that a patient experiences. If one questions a patient regarding the number of attempts at intercourse over the past week or the presence of morning erections, function is being addressed. Alternatively, if one queries the patient concerning the degree of problems that he has experienced due to his sexual dysfunction, bother is being measured. Gill and Feinstein (8) performed an extensive review of the literature and determined that the vast majority of HRQOL instruments only assess 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, as will be discussed later in the chapter.

2 The Effect of Prostate Cancer Diagnosis on Generic Quality of Life

It is well-understood that men with prostate cancer face disease-specific HRQOL concerns that include urinary, bowel, and sexual dysfunctions (9,10). In addition to these physical aspects of HRQOL, mental health concerns also play an important role and can have a major impact on HRQOL. It is not surprising that many patients experience high levels of distress when coping with cancer. To this end, one might expect that the diagnosis of prostate cancer in and of itself may have an effect on generic or disease-specific HRQOL. A review of the available literature, however, indicates that this is not the case.

In the disease-specific domains, there is no substantial evidence that the diagnosis of prostate cancer itself leads to HRQOL changes. In 2007, the vast majority of prostate cancer survivors are diagnosed with localized disease and, therefore, have minimal or no symptoms (11). Therefore, one would not expect significant HRQOL

changes immediately following a new diagnosis. However, there is no adequately sized completed study that has assessed men during pre-screening/diagnosis and then followed them through their disease course. As such, the available evidence on the impact of prostate cancer diagnosis on QOL comes from the studies that have assessed men post-diagnosis and pre-treatment, or studies that included an active surveillance cohort.

The available evidence suggests that urinary, bowel, or sexual functions are not directly affected by diagnosis or by the onset of the disease. In a study of 214 men with prostate cancer who were compared to 273 age-matched controls, Litwin et al. (12) found no difference in urinary function or bowel function of men with prostate cancer who elected observation only versus the age-matched controls. These results are supported by the results from Lubeck and colleagues (13) who conducted longitudinal assessments of 692 men with prostate cancer. In this study, men in the observation only group ($n=87$) reported few urinary or bowel difficulties at the time of diagnosis, 1 year post-diagnosis, or 2 years post-diagnosis. Hoffman and colleagues (14) analyzed the HRQOL responses of 293 men from the New Mexico component of the PCOS cohort and compared them to 618 healthy controls matched on age and ethnicity. The unique characteristic of the PCOS cohort in general and the New Mexico component specifically is that the study is population-based (meaning that all men in a geographic region who had the disease were included in the study regardless of where they received treatment, minimizing selection bias) and that the study is the longest and largest longitudinal study of its kind, making it a singular resource for addressing questions regarding quality of life in prostate cancer. In the New Mexico study, the PCOS researchers found that the prostate cancer patients reported significantly better baseline urinary control and less urinary bother. No significant differences were noted in the sexual or bowel domains at baseline. Similarly, Bacon et al. (10) compared general HRQOL in 783 men with incident prostate cancer to 1,928 age-matched healthy controls. They found that the men with localized prostate cancer actually reported significantly better physical function and less bodily pain (both $p < 0.0002$) than the healthy controls but had worse general health, vitality, social function, and role limitations due to physical and emotional problems (all p values < 0.004). The observation from the Hoffman (14) and Bacon (10) studies that men with newly diagnosed prostate cancer appear to have better baseline HRQOL in certain domains is likely due to a “healthy screenee” bias. In other words, healthier and more robust men are more likely to undergo prostate cancer screening, which results in these men having better baseline function than age-matched controls. This “healthy screenee” bias has also been observed in the SEER-Medicare dataset (15). Taken as a whole, these studies appear to indicate that a new diagnosis of prostate cancer does not appear to have a deleterious effect on disease-specific HRQOL.

Although the results above seem to indicate otherwise, there are some authors who argue that sexual function may be impacted by diagnosis or to some extent be linked to the nature of the disease (9). These authors point to the results from a handful of comparison studies that indicate that men diagnosed with prostate

cancer and who opted for watchful waiting report reduced sexual function when compared to age-matched controls. In a comparison group design, Helgason et al. (16) assessed 342 men with prostate cancer and 314 health age-matched controls. The 139 men in the observation group reported more sexual dysfunction and more distress over this dysfunction than did the men in the control group. In the Litwin et al. (12) study, the observation group also reported lower sexual function than the age-matched controls. There are two points to bear in mind when considering these results. Firstly, patients who elect observation often have more co-morbid disease (17). Neither of these studies controlled for co-morbidities and, therefore, selection bias may be responsible for the findings. The other point to remember when considering these reports is that the time since diagnosis of the observation groups ranged from 2 to 5 years suggesting that these symptoms may be related to disease sequela as opposed to a reaction to diagnosis (9). Given these points, it is likely that the diagnosis of prostate cancer itself has little or no effect on disease-specific HRQOL.

In terms of the generic HRQOL domains, there is no evidence that the diagnosis of prostate cancer affects these domains. In the studies previously cited, there were no differences found in the generic domains of the SF-36 in men diagnosed with prostate cancer when compared to age-matched controls. In fact, it appears that the various prostate cancer treatments have little effect on long-term generic HRQOL outcomes either. Penson et al. (18) studied 2,693 men newly diagnosed with localized prostate cancer in the PCOS cohort who had baseline (diagnosis) and 2-year HRQOL data. No differences in 2-year general HRQOL outcomes were noted among the various treatments for localized prostate cancer. Potosky et al. (19) observed similar findings at 5 years. In the 2-year study, Penson et al. (18) noted that men with sexual and urinary dysfunctions had significantly worse outcomes in the bodily pain, mental health, role limitation, vitality, and overall health status domains of general HRQOL, when controlling for baseline function, treatment and 27 other co-variables, indicating that impotence and incontinence negatively impact HRQOL. This underscores the need to understand the incidence of erectile dysfunction following prostate cancer treatment and its effect on HRQOL. We will explore this further later in this chapter.

3 The Psychological Effect of a New Prostate Cancer Diagnosis

Although the diagnosis of prostate cancer itself does not appear to directly affect generic HRQOL, this is not to say it has no effect at all. In fact, the diagnosis of prostate cancer likely has a significant effect on the psychological functioning of the patient, which in turn will affect quality of life. It may be that generic HRQOL instruments, such as the SF-36 (20) or the FACT-G (21) simply are not precise enough to capture this impact. To this end, other more psychologically oriented instruments may be more useful for measuring this effect.

There is little doubt that the diagnosis of cancer may bring with it significant distress (22,23). The number of cancer patients who report clinically significant distress has been estimated to range from 34 to 46% (22). An elevation in distress and anxiety is considered normal and expected as patients and their families attempt to understand the diagnosis and consider options for treatment. In general, the trajectory is such that this distress peaks at diagnosis and treatment decision, and then for many patients, tends to dissipate to normal or subthreshold levels as patients and their families accommodate to the cancer diagnosis and treatment implications (24). This is especially true for patients diagnosed with treatable disease, and specifically demonstrated in studies of men with early stage prostate cancer (24–28).

When men with prostate cancer do experience distress, the literature suggests that these men primarily manifest their distress in anxiety and depression with the focus primarily on anxiety. For example, in a study of 121 both early and late prostate cancer patients who were on average 4 years post-diagnosis, Roth and colleagues (29) found that 33% of these men scored at or above the anxiety cut-off score of the Hospital Anxiety and Depression Scale (HADS) (30), while a lower (although still clinically elevated) 15% of men scored at or above the cut-off score for depression on the HADS. These results are confirmed in another cross-sectional study conducted by Balderson and Towell (31) who surveyed 94 men in the United Kingdom with various stages of prostate cancer. These men were on average 2–3 years post-diagnosis. These researchers found that overall 38% of the men were experiencing distress as measured by the HADS, and this sample exhibited a higher mean anxiety score (7.17) as compared to a mean depression score (5.09). These results have directed the research investigating the psychological impact of prostate cancer to focus more closely on anxiety as opposed to depression.

Over the past 10 years, a handful of studies have assessed distress and anxiety at diagnosis, providing preliminary evidence of the impact of prostate cancer diagnosis on the psychological state of the patient. Nordin et al. (32) assessed 118 Swedish prostate cancer patients with the Hospital Anxiety and Depression Scale. At diagnosis, 12% of the patients reported scores at or above the cut-off for anxiety and the same percentage scored significantly for depression. As expected, these rates were higher for those diagnosed with advanced disease as compared to localized disease. Of those diagnosed with advanced disease, 18% reported anxiety and 15% reported depressive symptoms. This is in contrast to localized disease where 9% reported anxiety and 10% reported depression. In a study of 88 men with newly diagnosed clinically localized prostate cancer, Bisson et al. (33) reported that 22% of men had meaningful levels of anxiety as measured with the HADS, and 5% reported significant depressive symptoms. In a recent study, Korfage et al. (27) studied 299 men with newly diagnosed localized prostate cancer from the Netherlands. These men were assessed with the state subscale of the State Trait Anxiety Inventory. The use of this scale confirmed the high rates of anxiety reported with the HADS in previous studies as 28% of men reported scores of anxiety above the cut-off score of the STAI-state.

Although none of these studies assessed men before the diagnosis of prostate cancer, these rates of distress and anxiety are generally considered elevated and indicate

that the diagnosis of prostate cancer increases distress in these men. This conclusion is supported by a recent article published by Korfage et al. (26) who assessed 3,800 men pre-screening with the mental health subscale of the SF-36 Quality of Life measure. The authors then followed these men longitudinally and 52 men were diagnosed with prostate cancer as a result of the screening. These researchers re-administered the questionnaire to these 52 diagnosed men before initial treatment and then 6 months following treatment. The SF-36 mental health subscale does not produce “caseness” (i.e., the percentage of men scoring above a cut-off), but these authors did find a significant decrease in men’s mental health scores (indicating a decline in mental health functioning) from the pre-screening assessment to the assessment just before initial treatment. This scale specifically assesses mental health items such as feeling nervous, down, and depressed. At the assessment 6 months after treatment, the mental health scores had elevated to the point of no significant difference between baseline scores as compared to the 6-month follow-up score. In summary, while there appears to be little long-term psychological effect of prostate cancer in men with localized disease, patients not surprisingly experience significant psychological distress and anxiety in the period immediately following diagnosis.

4 The Effect of Post-treatment Sexual Dysfunction on Quality of Life

Sexual dysfunction can occur after all treatments for prostate cancer usually as a result of nerve or vascular injury (in the case of surgery or radiation) or endocrinologic abnormalities (following hormone ablation therapy). Although numerous different forms of sexual dysfunction can occur following treatment, including erectile dysfunction, ejaculatory dysfunction, and libido disturbances, we will focus primarily on erectile dysfunction (ED), as it is the best studied of the sexual dysfunctions that occur after treatment for prostate cancer. Given the earlier observation from the PCOS study that erectile dysfunction is independently associated with worse generic HRQOL 2 years following the diagnosis of prostate cancer (18), it is important to understand the incidence of dysfunction and its effect on disease-specific HRQOL after each commonly used therapy for prostate cancer.

4.1 Radical Prostatectomy

Impotence occurs fairly commonly after radical prostatectomy (34). Erectile dysfunction following surgery rates are likely related to a number of factors, including pre-operative function (35), stage of the cancer (36), age of health of the patient (35), and potentially the operating surgeon (37). To this end, while reports from single high-volume centers likely represent optimal outcomes, it is better to review

data from multi-center studies and population-based projects. To date, the largest population-based report of longitudinal outcomes following radical prostatectomy comes from the PCOS (38). Penson et al. (39) studied outcomes in the 1,213 men in PCOS who underwent radical prostatectomy for localized prostate cancer and were followed for 5 years. At baseline, 81% of patients reported erections firm enough for intercourse. This high-baseline potency rate is likely due to a combination of factors, including a “healthy screenee” bias and selection bias, as sicker men are less likely to be offered surgery. Six months following diagnosis (and surgery), only 9% of patients report erections firm enough for intercourse. This improved to 17% at 12 months, 22% at 2 years and 28% at 5 years. It is interesting to consider the proportion of patients reporting that their sexual dysfunction was a moderate to big problem in this study. At baseline, 20% of patients reported that their sexual dysfunction was a moderate to big problem, corresponding nicely to a 19% ED rate. At 6 months, 70% report that it was a moderate to big problem, which is less than the 91% who report that their erections were not firm enough for intercourse. While the degree of ED improved somewhat at years 1, 2, and 5, it is interesting to note that the amount of bother that the dysfunction caused improves with time. At 12 months, 61% stated it was a moderate to big problem; at 24 months, 54%, and at 60 months, 46%. This underscores the fact that function and bother do not correlate in the sexual domains in prostate cancer patients.

Other authors have noted a similar relationship between sexual function and bother following radical prostatectomy. Bates et al. (40) assessed HRQOL in 83 men who underwent radical retropubic prostatectomy using the ICS-male questionnaire. Of the 74 men who reported pre-operative potency, 44 (59%) were completely impotent. However, 45% of these impotent men reported that this was not a problem and 20% reported it was only a “bit of a problem.” It should be noted that this finding is not limited to the post-prostatectomy setting. In a study of 528 men, including 214 men with localized prostate cancer who underwent either surgery, radiotherapy, or watchful waiting, and 273 controls, level of sexual function was compared to degree of bother experienced (12). Although there was reasonable correlation (90% of men with good or very good sexual function experienced none, or very little bother, while 78% with poor or very poor sexual function experienced great bother from their condition), there were still a considerable number of patients in whom function and bother did not agree.

It is interesting to consider why some patients experience significant erectile dysfunction yet report little or no bother from their condition. One possible explanation for the discordance between function and bother in prostate cancer patients is the psychological ability for patients to “rationalize away” their ED by reassuring themselves that they are “cured” of cancer. To explore this hypothesis, Penson and colleagues (41) compared HRQOL outcomes in 121 men without prostate cancer who had ED to 47 men with ED with a history of prostate cancer and its treatment. The prostate cancer group reported significantly worse sexual self-efficacy, erectile function, intercourse satisfaction, and orgasmic function than impotent men without prostate cancer. However, the impotent prostate cancer survivors reported significantly less psychological impact of erectile dysfunction on both sexual

experience and emotional life than impotent men without prostate cancer. These findings appear to support the hypothesis that the psychological relief of knowing that one's prostate cancer has been successfully treated may mitigate the deleterious HRQOL effects of erectile dysfunction. All of these studies underscore the need to approach each patient individually, as each patient experiences sexual dysfunction in a profoundly personal manner, and treatment plans need to be designed around patients' psychological needs and clinical expectations.

The studies above do not specifically address the effectiveness of nerve-sparing in maintaining sexual function. To explore the effect of the nerve-sparing RP technique on quality of life outcomes, Talcott et al. (42) 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 any type of nerve-sparing procedure had worse sexual function than had been previously reported. Furthermore, they noted no statistically significant differences in sexual functioning between the nerve-sparing and non-nerve-sparing groups. This study, however, reports a single center experience and may not be representative of what occurs in other centers or in the community at large. In the PCOS study mentioned above, a limited analysis was performed to assess the effectiveness of nerve-sparing (39). Men who underwent bilateral nerve-sparing surgery were more likely to report erections firm enough for intercourse at 60 months (40%) than those who underwent unilateral nerve-sparing (23%) or non-nerve-sparing (23%) surgery ($p = 0.01$). The effectiveness of nerve-sparing was closely associated with age at the time of surgery ($p < 0.001$). In a report from CaPSURE, Litwin et al. (43) compared longitudinal HRQOL in 218 men who underwent nerve-sparing RP with 124 men who underwent the non-nerve-sparing technique. They found that the patients who underwent nerve-sparing surgery had significantly better sexual function than those who had non-nerve-sparing surgery at 6, 12, and 18 months following treatment, although the overall level of sexual function was low for both groups. These two studies confirm that nerve-sparing surgery appears to positively impact sexual outcomes.

Finally, numerous randomized clinical trials have documented the effectiveness of phosphodiesterase type-5 inhibitors (PDE5i) in aiding erectile function following bilateral and unilateral nerve-sparing radical prostatectomies (44). As this is discussed elsewhere in this book, we will not go into great detail in the current chapter. However, it is interesting to contrast the findings of these randomized clinical trials to a large population-based cohort of men who elected to try sildenafil as part of routine clinical care. In randomized, blinded trials from the Cleveland Clinic, for example, 72% of patients who underwent bilateral nerve-sparing radical prostatectomy reported erections firm enough for vaginal penetration (44). This population represents a group of highly motivated and selected men who had their surgery at a high-volume center that is known for superior results. In the general community, where patients' expectations may not be appropriate and where the quality of the surgery may not be as high, the results are not as encouraging. In the 520 men from the PCOS cohort who underwent radical prostatectomy and tried sildenafil and were followed for 5 years, only 45% reported that the drug helped a lot or somewhat. The

amount that the drug helped was closely related to the patient's age, with 63% of men under the age of 55 years, 59% of men aged 55–60 years, 30% of men aged 60–64 years, 40% of men aged 65–70 years, and 32% of men over the age of 70 years reporting it helped a lot or somewhat (45). In summary, oral PDE5i appear to be effective in aiding erectile function in men after radical prostatectomy, but probably to a lesser degree than what has been reported in clinical trials.

In summary, it is incumbent upon providers to help patients set reasonable expectations regarding erectile function after surgery. Specifically, it can take 1–2 years for functional erections to return. In addition, while oral agents are effective in restoring erectile function, they may be less effective than has been reported in randomized clinical trials, particularly in older patients. With proper counseling, it is likely that the negative effect of sexual dysfunction on HRQOL following surgery for prostate cancer can be minimizing.

4.2 External Beam Radiotherapy

Sexual dysfunction can occur following both external beam radiotherapy and interstitial brachytherapy (seeds), presumably due to radiation injury to the neurovascular bundles adjacent to the prostate, arterial inflow conduits, and erectile tissue. Because the basic techniques of external beam radiotherapy have been in use for decades, there is considerably more information regarding sexual dysfunction and HRQOL after XRT. Mantz et al. (46) 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.

It is interesting to note that, similar to the situation following surgery, the effect of sexual dysfunction on quality of life is highly individualized. Reddy et al. (47) 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. Helgason et al. (48) studied 53 men who had undergone external beam radiotherapy 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. However, only 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 also found that sexual dysfunction has less of an effect on quality of life following external beam radiotherapy. Caffo et al. (49) showed that, although 44% of men had significant sexual dysfunction following external beam radiotherapy, general quality of life, measured as physical, psychological, and relational well-being, all remained good.

In summary, erectile dysfunction also occurs commonly after external beam radiotherapy, although based on the currently available literature, perhaps to a somewhat lesser extent than in surgical patients. However, like surgical patients, function and bother do not always correlate and many patients who experience sexual dysfunction following external beam radiotherapy do not report concordant bother.

4.3 Interstitial Brachytherapy (Seeds)

Although data related to brachytherapy are relatively immature and are limited by short follow-up, it appears that this treatment may also effect erectile function and disease-specific HRQOL. Initial reports indicated that IB had minimal effect on sexual function. Arterberry et al. (50) reported that 87% of 35 patients who were potent pre-treatment maintained their potency 6 months following treatment. However, this study had relatively small numbers of patients and limited follow-up. In a study directly comparing outcomes between men undergoing surgery and IB and age-matched controls, Brandeis et al. (51) found that, at 3–17 months following treatment, sexual function in the IB group was significantly worse than in age-matched controls. There were no significant differences between the surgical and brachytherapy groups in the sexual domains. Recent reports from the CaPSURE database indicate that, while sexual function 3–4 years after seed implantation is significantly better than similar patients undergoing surgery or external beam radiotherapy, there is still a significant decline in sexual function in the seeds group from baseline. In addition, although there are significant differences in sexual function between the three groups at 4 years after therapy, there are no differences in either (52).

5 The Psychological Effect of Post-treatment Sexual Dysfunction

In addition to the HRQOL implications discussed above, it is also important to consider the psychological impact of struggling with erectile dysfunction. In contrast to the research on coping with the diagnosis of prostate cancer, which has focused primarily on anxiety, the literature describing the psychological impact of ED concentrates on depression. Although little, if any, data exist on the association between erectile dysfunction and depression specifically in men with prostate cancer, it is clear from studies conducted in other settings that there is a relationship between these two variables. Shabsigh and colleagues (53) studied 120 with ED and/or benign prostatic hyperplasia (BPH). This study grouped men in three categories: 48 men with ED only, 34 men with BPH only, and 18 men with both ED and BPH. The average age of the men in the study was approximately 56 years old, and depressive symptoms were measured with the Beck Depression Inventory (BDI) (54). These researchers found a remarkably high rate of depressive symptoms (56%) in the ED only group and the ED plus BPH group. This rate of 56% was significantly higher than the 21% of subjects who reported depressive symptoms in the BPH only group. These results are supported by two population-based studies that have also researched the association between depression and erectile dysfunction. Araujo et al. (55) presented data on 1,700 subjects from the Massachusetts Male Aging Study, a large, population-based study of the men from the greater Boston area. The men in the study ranged in age from 40 to 70 years old. In this study, the researchers

measured ED with a single, self-report question and depression with the Center for Epidemiological Studies Depression Scale (CES-D) (56). After controlling for variables such as age, health status, and medication use, depressive symptoms were clearly and significantly associated with ED (OR 1.8). Very similar results were reported by Nicolosi et al. (57) in a population-based study of 1,800 subjects from Brazil, Japan, and Malaysia. These subjects also ranged in age from 40 to 70 years old, and ED was measured with a single, self-report question while depression was assessed with the CES-D. These researchers also found a significant association between depressive symptoms and erectile dysfunction (OR 1.7).

A difficult aspect in studying this association is trying to determine which variable comes first. Does depression cause ED, or does ED cause depression? Shiri and colleagues (58) have suggested that it is a bidirectional relationship. These authors reported results from the large, population-based, longitudinal study conducted in Finland. The 1,680 subjects in this study ranged in age from 50 to 70 years. ED was assessed with two self-report questions and depression was measured by the 5-item Mental Health Inventory (59). In this study, the incidence of depression was higher in those men who had ED as compared to men without ED ($p < 0.01$). Likewise, the incidence of ED was higher in men who reported depression than those who did not report depression ($p < 0.05$). The authors point to these results as evidence of a bidirectional relationship between erectile dysfunction and depression.

There are few, if any, studies that have researched this question in men with prostate cancer. Clinical experience certainly supports that the association between ED and depression exists in men treated for prostate cancer. Interestingly, there may be reason to believe men treated for prostate cancer will cope more effectively with erectile dysfunction as compared to men without prostate cancer. Penson et al. (41) provide preliminary evidence for this in their study discussed above. These authors suggest that men treated for prostate cancer may be able to place their ED in perspective in relation to the importance of dealing with their cancer. Additionally, many healthy men who experience ED often blame themselves; thinking that a lack of “manliness” is at fault for the loss of erections. Although many men treated for prostate cancer feel less like a “man” if they experience ED, they do not have the added psychological burden of blaming themselves for the loss of erections. The treatment clearly impacts erectile functioning and these men may possibly adjust more effectively to erectile dysfunction as a result.

6 Conclusions

Quality of life is an important concern for men with prostate cancer. The effect of this disease and the side-effects of its treatment on health-related quality of life in prostate cancer survivors cannot be understated. The literature indicates that, while the majority of men with prostate cancer do not experience significant declines in generic HRQOL directly due to the disease, a new diagnosis often causes significant psychological distress and anxiety, which can transiently have negative effects

on HRQOL. While there are numerous side-effects of treatment which can affect HRQOL, sexual dysfunction, specifically erectile dysfunction, is among the most studied. While this condition is common after all therapies for prostate cancer, its HRQOL impact varies from patient to patient, based upon age, personal expectation, and the individual's psychological coping mechanisms. As healthcare providers, it is important that we be aware of the potential HRQOL impact of sexual dysfunction in prostate cancer survivors and attempt to make effective interventions to improve outcomes in these patients.

References

1. Jemal, A., Siegel, R., Ward, E., Murray, T., Xu, J., and Thun, M.J. (2007) Cancer statistics, 2007. *CA Cancer J. Clin.* **57**(1), 43–66.
2. Etzioni, R., Penson, D.F., Legler, J.M., et al. (2002) Overdiagnosis due to prostate-specific antigen screening: lessons from U.S. prostate cancer incidence trends. *J. Natl. Cancer Inst.* **94**(13), 981–990.
3. Singer, P.A., Tasch, E.S., Stocking, C., Rubin, S., Siegler, M., and Weichselbaum, R. (1991) Sex or survival: trade offs between quality and quantity of life. *J. Clin. Oncol.* **9**(2), 328–334.
4. Patrick, D.L., and Erickson, P. (1993) Assessing health-related quality of life for clinical decision-making. In: Walker, S.R., and Rosser, R.M., eds. *Quality of Life Assessment: Key Issues in the 1990's*. Dordrecht: Kluwer Academic Publishers, Chap. 19.
5. Litwin, M.S., Lubeck, D.P., Henning, J.M., and Carroll, P.R. (1998) Differences in urologist and patient assessments of health related quality of life in men with prostate cancer: results of the CaPSURE database. *J. Urol.* **159**(6), 1988–1992.
6. Litwin, M.S., and McGuigan, K.A. (1999) Accuracy of recall in health-related quality-of-life assessment among men treated for prostate cancer. *J. Clin. Oncol.* **17**(9), 2882–2888.
7. Legler, J., Potosky, A.L., Gilliland, F.D., Eley, J.W., and Stanford, J.L. (2000) Validation study of retrospective recall of disease-targeted function: results from the prostate cancer outcomes study. *Med. Care* **38**(8), 847–857.
8. Gill, T.M., and Feinstein, A.R. (1994) A Critical appraisal of the quality-of-life measurements. *JAMA*; **272**(8), 619–626.
9. Eton, D.T., and Lepore, S.J. (2002) Prostate cancer and health-related quality of life: a review of the literature. *Psycho-Oncology* **11**(4), 307–326.
10. Bacon, C.G., Giovannucci, E., Testa, M., Glass, T.A., and Kawachi, I. (2002) The association of treatment-related symptoms with quality-of-life outcomes for localized prostate carcinoma patients. *Cancer* **94**(3), 862–871.
11. Cooperberg, M.R., Lubeck, D.P., Meng, M.V., Mehta, S.S., and Carroll, P.R. (2004) The changing face of low-risk prostate cancer: trends in clinical presentation and primary management. *J. Clin. Oncol.* **22**(11), 2141–2149.
12. Litwin, M.S., Hays, R.D., Fink, A., et al. (1995) Quality-of-life outcomes in men treated for localized prostate cancer. *JAMA* **273**(2), 129–35.
13. Lubeck, D.P., Litwin, M.S., Henning, J.M., Stoddard, M.L., Flanders, S.C., and Carroll, P.R. (1999) Changes in health-related quality of life in the first year after treatment for prostate cancer: results from CaPSURE. *Urology* **53**(1), 180–186.
14. Hoffman, R.M., Gilliland, F.D., Penson, D.F., Stone, S.N., Hunt, W.C., and Potosky, A.L. (2004) Cross-sectional and longitudinal comparisons of health-related quality of life between patients with prostate carcinoma and matched controls. *Cancer* **101**(9), 2011–2019.
15. Zeliadt, S.B., Etzioni, R., Ramsey, S.D., Penson, D.F., and Potosky, A.L. (2007) Trends in treatment costs for localized prostate cancer: the healthy screenee effect. *Med. Care* **45**(2), 154–159.

16. Helgason, A.R., Adolfsson, J., Dickman, P., Fredrikson, M., Arver, S., and Steineck, G. (1996) Waning sexual function – the most important disease-specific distress for patients with prostate cancer. *Br. J. Cancer* **73**(11), 1417–1421.
17. Harlan, L.C., Potosky, A., Gilliland, F.D., et al. (2001) Factors associated with initial therapy for clinically localized prostate cancer: prostate cancer outcomes study. *J. Natl. Cancer Inst.* **93**(24), 1864–1871.
18. Penson, D.F., Feng, Z., Kuniyuki, A., et al. (2003) General quality of life 2 years following treatment for prostate cancer: what influences outcomes? Results from the prostate cancer outcomes study. *J. Clin. Oncol.* **21**(6), 1147–1154.
19. Potosky, A.L., Davis, W.W., Hoffman, R.M., et al. (2004) Five-year outcomes after prostatectomy or radiotherapy for prostate cancer: the prostate cancer outcomes study. *J. Natl. Cancer Inst.* **96**(18), 1358–1367.
20. Ware, J.E., Jr., and Sherbourne, C.D. (1992) The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med. Care* **30**(6), 473–483.
21. Cella, D.F., Tulsky, D.S., Gray, G., et al. (1993) The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. *J. Clin. Oncol.* **11**(3), 570–579.
22. Ellman, R., Angeli, N., Christians, A., Moss, S., Chamberlain, J., and Maguire, P. (1989) Psychiatric morbidity associated with screening for breast cancer. *Br. J. Cancer* **60**(5), 781–784.
23. Ford, S., Fallowfield, L., Hall, A., and Lewis, S. (1995) The influence of audiotapes on patient participation in the cancer consultation. *Eur. J. Cancer* **31A**(13–14), 2264–2269.
24. Davison, B.J., and Goldenberg, S.L. (2003) Decisional regret and quality of life after participating in medical decision-making for early-stage prostate cancer. *BJU Int.* **91**(1), 14–17.
25. Dale, W., Bilir, P., Han, M., and Meltzer, D. (2005) The role of anxiety in prostate carcinoma: a structured review of the literature. *Cancer* **104**(3), 467–478.
26. Korfage, I.J., de Koning, H.J., Roobol, M., Schroder, F.H., and Essink-Bot, M.L. (2006) Prostate cancer diagnosis: the impact on patients' mental health. *Eur. J. Cancer* **42**(2), 165–170.
27. Korfage, I.J., Essink-Bot, M.L., Janssens, A.C., Schroder, F.H., and de Koning, H.J. (2006) Anxiety and depression after prostate cancer diagnosis and treatment: 5-year follow-up. *Br. J. Cancer* **94**(8), 1093–1098.
28. Korfage, I.J., Hak, T., de Koning, H.J., and Essink-Bot, M.L. (2006) Patients' perceptions of the side-effects of prostate cancer treatment – a qualitative interview study. *Soc. Sci. Med.* **63**(4), 911–919.
29. Roth, A.J., Kornblith, A.B., Batel-Copel, L., Peabody, E., Scher, H.I., and Holland, J.C. (1998) Rapid screening for psychologic distress in men with prostate carcinoma: a pilot study. *Cancer* **82**(10), 1904–1908.
30. Zigmond, A.S., and Snaith, R.P. (1983) The hospital anxiety and depression scale. *Acta Psychiatr. Scand.* **67**(6), 361–370.
31. Balderson, N., and Towell, T. (2003) The prevalence and predictors of psychological distress in men with prostate cancer who are seeking support. *Br. J. Health Psychol.* **8**(Pt 2), 125–134.
32. Nordin, K., Berglund, G., Glimelius, B., and Sjoden, P.O. (2001) Predicting anxiety and depression among cancer patients: a clinical model. *Eur. J. Cancer* **37**(3), 376–384.
33. Bisson, J.I., Chubb, H.L., Bennett, S., Mason, M., Jones, D., and Kynaston, H. (2002) The prevalence and predictors of psychological distress in patients with early localized prostate cancer. *BJU Int.* **90**(1), 56–61.
34. Penson, D.F., Litwin, M.S., and Aaronson, N.K. (2003) Health related quality of life in men with prostate cancer. *J. Urol.* **169**(5), 1653–1661.
35. Wei, J.T., Dunn, R.L., Marcovich, R., Montie, J.E., and Sanda, M.G. (2000) Prospective assessment of patient reported urinary continence after radical prostatectomy. *J. Urol.* **164**(3 Pt 1), 744–748.
36. Eastham, J.A., Kattan, M.W., Rogers, E., et al. (1996) Risk factors for urinary incontinence after radical prostatectomy [see comments]. *J. Urol.* **156**(5), 1707–1713.
37. Ellison, L., Heaney, J., and Birkmeyer, J. (2000) The effect of hospital volume on mortality and resource use after radical prostatectomy. *J. Urol.* **163**(3), 867–869.

38. Potosky, A.L., Harlan, L.C., Stanford, J.L., et al. (1999) Prostate cancer practice patterns and quality of life: the Prostate Cancer Outcomes Study. *J. Natl Cancer Inst.* **91**(20), 1719–1724.
39. Penson, D.F., McLerran, D., Feng, Z., et al. (2005) Five-year urinary and sexual outcomes after radical prostatectomy: results from the Prostate Cancer Outcomes Study. *J. Urol.* **173**(5), 1701–1705.
40. Bates, T.S., Wright, M.P., and Gillatt, D.A. (1998) Prevalence and impact of incontinence and impotence following total prostatectomy assessed anonymously by the ICS-male questionnaire. *Eur. Urol.* **33**(2), 165–169.
41. Penson, D.F., Latini, D.M., Lubeck, D.P., Wallace, K., Henning, J.M., and Lue, T. (2003) Is quality of life different for men with erectile dysfunction and prostate cancer compared to men with erectile dysfunction due to other causes? Results from the ExCEED data base. *J. Urol.* **169**(4), 1458–1461.
42. Talcott, J.A., Rieker, P., Propert, K.J., et al. (1997) Patient-reported impotence and incontinence after nerve-sparing radical prostatectomy. *J. Natl. Cancer Inst.* **89**(15), 1117–1123.
43. Litwin, M.S., Flanders, S.C., Pasta, D.J., Stoddard, M.L., Lubeck, D.P., and Henning, J.M. (1999) Sexual function and bother after radical prostatectomy or radiation for prostate cancer: multivariate quality-of-life analysis from CaPSURE. Cancer of the Prostate Strategic Urologic Research Endeavor. *Urology* **54**(3), 503–508.
44. Zippe, C.D., Kedia, A.W., Kedia, K., Nelson, D.R., and Agarwal, A. (1998) Treatment of erectile dysfunction after radical prostatectomy with sildenafil citrate (Viagra). *Urology* **52**(6), 963–966.
45. Penson, D.F., McLerran, D., Feng, Z., et al. (2005) 5-year urinary and sexual outcomes after radical prostatectomy: results from the prostate cancer outcomes study. *J. Urol.* **173**(5), 1701–1705.
46. Mantz, C.A., Song, P., Farhangi, E., et al. (1997) Potency probability following conformal megavoltage radiotherapy using conventional doses for localized prostate cancer. *Int. J. Radiat. Oncol. Biol. Phys.* **37**(3), 551–557.
47. Reddy, S.M., Ruby, J., Wallace, M., and Forman, J.D. (1997) Patient self-assessment of complications and quality of life after conformal neutron and photon irradiation for localized prostate cancer. *Radiat. Oncol. Investig.* **5**(5), 252–256.
48. Helgason, A.R., Fredrikson, M., Adolfsson, J., and Steineck, G. (1995) Decreased sexual capacity after external radiation therapy for prostate cancer impairs quality of life. *Int. J. Radiat. Oncol. Biol. Phys.* **32**(1), 33–39.
49. Caffo, O., Fellin, G., Graffer, U., and Luciani, L. (1996) Assessment of quality of life after radical radiotherapy for prostate cancer. *Br. J. Urol.* **78**(4), 557–563.
50. Arterbery, V.E., Frazier, A., Dalmia, P., Siefer, J., Lutz, M., and Porter, A. (1997) Quality of life after permanent prostate implant. *Semin. Surg. Oncol.* **13**(6), 461–464.
51. Brandeis, J.M., Litwin, M.S., Burnison, C.M., and Reiter, R.E. (2000) Quality of life outcomes after brachytherapy for early stage prostate cancer. *J. Urol.* **163**(3), 851–857.
52. Huang, G.J., Sadetsky, N., Carroll, P., and Penson, D.F. (2007) Predictors of HRQOL during long-term follow-up of men treated for prostate cancer. In: *2007 Prostate Cancer Symposium*, Orlando, FL.
53. Shabsigh, R.R., Klein, L.L.T., Seidman, S.S., Kaplan, S.S.A., Lehrhoff, B.B.J., and Ritter, J.J.S. (1998) Increased incidence of depressive symptoms in men with erectile dysfunction. *Urology* **52**(5), 848–852.
54. Schneider, B.B., and Varghese, R.R.K. (1995) Scores on the SF-36 scales and the Beck Depression Inventory in assessing mental health among patients on hemodialysis. *Psychol. Rep.* **76**(3 Pt 1), 719–722.
55. Araujo, A.A.B., Durante, R.R., Feldman, H.H.A., Goldstein, I.I., and McKinlay, J.J.B. (1998) The relationship between depressive symptoms and male erectile dysfunction: cross-sectional results from the Massachusetts Male Aging Study. *Psycho. Med.* **60**(4), 458–465.
56. van Wilgen, C.C.P., Dijkstra, P.P.U., Stewart, R.R.E., Ranchor, A.A.V., and Roodenburg, J.J.L.N. (2006) Measuring somatic symptoms with the CES-D to assess depression in cancer patients after treatment: comparison among patients with oral/oropharyngeal, gynecological, colorectal, and breast cancer. *Psychosomatics* **47**(6), 465–470.

57. Nicolosi, A.A., Moreira, E.D.E.D., Villa, M.M., and Glasser, D.B.D.B. (2004) A population study of the association between sexual function, sexual satisfaction and depressive symptoms in men. *J. Affec. Disord.* **82**(2), 235–243.
58. Shiri, R.R., Koskimäki, J.J., Tammela, T.L.T.L.J., Häkkinen, J.J., Auvinen, A.A., and Hakama, M.M. (2007) Bidirectional relationship between depression and erectile dysfunction. *J. Urol.* **177**(2), 669–673.
59. Rumpf, H.H.J., Meyer, C.C., Hapke, U.U., and John, U.U. (2001) Screening for mental health: validity of the MHI-5 using DSM-IV Axis I psychiatric disorders as gold standard. *Psychiatry Res.* **105**(3), 243–253.

Sexual Function in the Prostate Cancer Patient

Mulhall, J.P. (Ed.)

2009, XX, 268 p. 27 illus., 5 illus. in color., Hardcover

ISBN: 978-1-60327-554-5

A product of Humana Press