Survivorship: Sexual Dysfunction (Male), Version 1.2013


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Survivorship: Sexual Dysfunction (Male), Version 1.2013

Clinical Practice Guidelines in Oncology

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Overview
Cancer treatment, especially hormonal therapy and therapy directed toward the pelvis, can often impair sexual function. In addition, depression and anxiety, which are common in survivors, can contribute to sexual problems. Thus, sexual dysfunction is common in survivors and can cause increased distress and have a significant negative impact on quality of life.1–5 Nonetheless, sexual function is often not

Abstract
Various anticancer treatments, especially those directed toward the pelvis, can damage blood vessels and reduce circulation of blood to the penis and/or damage the autonomic nervous system, resulting in higher rates of erectile dysfunction in survivors than in the general population. In addition, hormonal therapy can contribute to sexual problems, as can depression and anxiety, which are common in cancer survivors. This section of the NCCN Guidelines for Survivorship provides screening, evaluation, and treatment recommendations for male sexual problems, namely erectile dysfunction. (J Natl Compr Canc Netw 2014;12:356–363)

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Disclosures for the NCCN Survivorship Oncology Panel
At the beginning of each NCCN Guidelines panel meeting, panel members review all potential conflicts of interest. NCCN, in keeping with its commitment to public transparency, publishes these disclosures for panel members, staff, and NCCN itself.

Individual disclosures for the NCCN Survivorship Panel members can be found on page 363. (The most recent version of these guidelines and accompanying disclosures are available on the NCCN Web site at NCCN.org.)

These guidelines are also available on the Internet. For the latest update, visit NCCN.org.

All recommendations are category 2A unless otherwise noted.

Clinical trials: NCCN believes that the best management for any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
Male Aspects of Sexual Dysfunction

The NIH Consensus Conference on Impotence defined impotence, or male erectile dysfunction (ED), as the inability to achieve or maintain an erection sufficient for satisfactory sexual performance. In fact, impotence and ED are not synonymous. Impotence can involve problems of sexual desire, orgasm, or ejaculation, which are not necessarily linked with achieving or maintaining an erection.

ED occurs frequently in the general population and increases with age. In one community-based study, 33% of men aged at least 75 years reported moderate or worse ED. ED is also very common in male cancer survivors. Anticancer treatment modalities used in a variety of cancers have the potential to damage blood vessels, leading to a reduction in blood circulation to the penis, and/or damage to the autonomic nervous system. Thus, higher rates of ED are seen in cancer survivors than in the general population. The prevalence of ED in male survivors of colorectal cancer has been reported to range from 45% to 75%, and it has been reported in up to 90% of prostate cancer survivors.
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DIAGNOSTIC EVALUATION

- Ask about sexual function at regular intervals
- Review present and past level of sexual activity and discuss the potential impact of therapy. Discuss any sexual concerns and how cancer treatment has affected sexual functioning and intimacy
- Discuss treatment-associated infertility if indicated, with appropriate urologic (male infertility) referrals
- Laboratory tests: HgbA1C, testosterone, creatinine, cholesterol
- Consider questionnaire as a primary screening tool for erectile dysfunction (ED) (eg, Sexual Health Inventory for Men [SHIM])

No concerns for sexual dysfunction

Concerns for sexual function

<table>
<thead>
<tr>
<th>H&amp;P</th>
<th>Sexual history (including prior problems)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Past medical and surgical histories</td>
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<tr>
<td></td>
<td>Identify traditional risk factors</td>
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<tr>
<td></td>
<td>(eg, cardiovascular disease, diabetes mellitus, smoking, alcoholism, obesity)</td>
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<tr>
<td></td>
<td>Psychosocial history</td>
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<tr>
<td></td>
<td>Including relationship status/issues, drug and alcohol use</td>
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<td></td>
<td>Screen for psychosocial concerns</td>
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<td></td>
<td>(See SANXDE-1† and NCCN Guidelines for Distress Management*)</td>
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<tr>
<td></td>
<td>Depression</td>
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<tr>
<td></td>
<td>Anxiety</td>
</tr>
<tr>
<td></td>
<td>Relationship issues</td>
</tr>
<tr>
<td>Oncologic history</td>
<td>Use of prescription and over-the-counter medications (especially hormone therapy or opioids)</td>
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<tr>
<td>Diagnosis/stage</td>
<td>Focused physical exam:</td>
</tr>
<tr>
<td>Surgeries</td>
<td>Chest (assess for gynecomastia)</td>
</tr>
<tr>
<td>Systemic treatment</td>
<td>Abdomen</td>
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<tr>
<td>Local RT</td>
<td>Genitourinary exam</td>
</tr>
<tr>
<td></td>
<td>(phallus, scrotum/testicles, cord structures)</td>
</tr>
<tr>
<td></td>
<td>Secondary sexual characteristics</td>
</tr>
<tr>
<td></td>
<td>Lower extremity pulses</td>
</tr>
</tbody>
</table>

*To view the most recent version of these guidelines, visit NCCN.org.
†Available online, in these guidelines, at NCCN.org.

Special consideration should be given to those men with androgen ablative therapy where testosterone replacement is ill-advised (ie, patient with advanced prostate cancer undergoing combination radiation/LHRH antagonist).
See Sexual Health Inventory for Men (SHIM) (SSFM-A).
INITIAL MANAGEMENT

The management of ED should be applied in a stepwise fashion, with increasing invasiveness of therapy as the failure rate increases and when the ED is not well tolerated.

The patient and, when possible, his partner should be informed of the relevant treatment options and their associated risks and benefits. Consider switching the dose before moving to second-line therapies.

SECOND-TIER MANAGEMENT

After the failure of first-line therapies, consider the following therapies. Before proceeding to other therapies, those with a failure of first-line PDE5i therapy should be evaluated to determine whether the trial of PDE5i was adequate. Consider switching the dose before moving to second-line therapies.

SECOND-TIER MANAGEMENT

Consider the following therapies for ED:

- Lifestyle modifications to improve vascular function such as smoking cessation, maintaining ideal body weight
- Avoiding excess alcohol consumption, and engaging in regular exercise
- Identifying sources for psychosocial dysfunction with appropriate referrals for psychosocial therapy or sexual counseling

SECOND-TIER MANAGEMENT

- Repeat evaluation and treatment with appropriate referrals for psychotherapy, sexual counseling as indicated
- Intramuscular self-injection therapy
- Intracavernosal self-injection therapy
- Oral phosphodiesterase type 5 (PDE5) inhibitors (e.g., sildenafil, tadalafil, vardenafil)
- Second trial of a similar PDE5i
- Second trial of a different PDE5i
- Intracavernosal vasoactive drug injection therapy (e.g., papaverine, phentolamine, prostaglandin E1)
- Intracavernosal alprostadil
- Local RT with erectile dysfunction
- Systemic treatment with erectile dysfunction
- Surgery with erectile dysfunction

SECOND-TIER MANAGEMENT

Identify sources for psychosocial dysfunction with appropriate referrals for psychotherapy or sexual counseling, including referral to a urologist. Consider the following therapies for ED:

SECOND-TIER MANAGEMENT

- Lifestyle modifications to improve vascular function such as smoking cessation, maintaining ideal body weight
- Avoiding excess alcohol consumption, and engaging in regular exercise
- Identifying sources for psychosocial dysfunction with appropriate referrals for psychosocial therapy or sexual counseling

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SEXUAL HEALTH INVENTORY FOR MEN (SHIM)

Sexual health is an important part of an individual's overall physical and emotional well-being. Erectile dysfunction (ED), also known as impotence, is a very common medical condition affecting sexual health. Fortunately, there are many different treatment options for ED. This questionnaire is designed to help you and your doctor identify if you may be experiencing erectile dysfunction. If you are, you may choose to discuss treatment options with your doctor.

Each question has several possible responses. Circle the number of the response that best describes your own situation. Please be sure that you select one and only one response for each question.

OVER THE PAST 6 MONTHS:

<table>
<thead>
<tr>
<th>Question</th>
<th>Very Low</th>
<th>Low</th>
<th>Moderate</th>
<th>High</th>
<th>Very High</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How do you rate your confidence you could get and keep an erection?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. When you had erections with sexual stimulation, how often were your erections hard enough for penetration (entering your partner)?</td>
<td>No sexual activity</td>
<td>Almost never or never</td>
<td>A few times (much less than half the time)</td>
<td>Sometimes (about half the time)</td>
<td>Most times (much more than, half the time)</td>
</tr>
<tr>
<td>3. During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?</td>
<td>Did not attempt intercourse</td>
<td>Almost never or never</td>
<td>A few times (much less than half the time)</td>
<td>Sometimes (about half the time)</td>
<td>Most times (much more than, half the time)</td>
</tr>
<tr>
<td>4. During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?</td>
<td>Did not attempt intercourse</td>
<td>Extremely difficult</td>
<td>Very difficult</td>
<td>Difficult</td>
<td>Slightly difficult</td>
</tr>
<tr>
<td>5. When you attempted sexual intercourse, how often was it satisfactory for you?</td>
<td>Did not attempt intercourse</td>
<td>Almost never or never</td>
<td>A few times (much less than half the time)</td>
<td>Sometimes (about half the time)</td>
<td>Most times (much more than, half the time)</td>
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</tbody>
</table>

**Provider Key:** Add the numbers corresponding to questions 1-5.

**Total:**

The SHIM further classifies ED severity with the following breakpoints:

1-7: Severe ED  
8-11: Moderate ED  
12-16: Mild to moderate ED  
17-21: Mild ED

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In 2005, the American Urological Association (AUA) published a guideline on the management of ED; it was reviewed and confirmed as still valid by the AUA in 2011.\textsuperscript{13} Using a consensus-based approach with the AUA guideline as a guide, the NCCN Survivorship Panel concluded that (1) informed patient and physician decision-making is the standard for guiding treatment decisions for ED treatment; and (2) a psychological overlay frequently exists in patients with ED and may be even more pronounced in the face of cancer survivorship. Endocrine disorders are also an important consideration in the cause of ED. Although sex therapy and the diagnosis and treatment of endocrine disorders are important management issues, these are beyond the scope of these guidelines and are therefore not addressed in depth.

**Evaluation and Assessment for Male Sexual Function**

Male cancer survivors should be asked about their sexual function at regular intervals. Patients should be asked about their sexual functioning before they received the cancer diagnosis, and their perceptions regarding the impact of cancer treatment on their sexual functioning and intimacy. A quantitative questionnaire such as the Sexual Health Inventory for Men can be considered to help identify patients who might benefit from treatment of ED.\textsuperscript{14}

Patients with concerns about their sexual function should undergo a more thorough evaluation, including screening for possible psychosocial problems (ie, anxiety, depression, relationship issues, drug or alcohol use) that can contribute to sexual dysfunction. Identifying prescription and over-the-counter medications (especially hormone therapy or opioids) that could be a contributing factor is also important. A focused physical examination can also be helpful and should include examination of the chest (for gynecomastia), abdomen, phallus, scrotum/testicles, and cord structures.

Importantly, cardiovascular risk should be estimated for all men with ED, especially those with cardiovascular disease. Cardiovascular disease and ED share risk factors and often coexist.\textsuperscript{23} Sexual activity is considered equivalent to walking 1 mile in 20 minutes on a flat surface or to climbing 2 flights of stairs in 20 seconds.\textsuperscript{23} Men who cannot perform these exercises without symptoms are considered to be at high risk for experiencing adverse events associated with sexual activity and should be referred to a cardiologist before treatment for ED.\textsuperscript{23}

**Interventions for Male Sexual Dysfunction**

Treatment for ED begins with modification of risk factors, such as smoking cessation, weight loss, increasing physical activity, and avoiding excess alcohol consumption. In addition, treatment of psychosocial problems, with referral to sex and couples therapy as appropriate, can often alleviate symptoms of ED.

Oral phosphodiesterase type 5 inhibitors (PDE5is) have been shown to improve the symptoms of ED and be well tolerated.\textsuperscript{8,10} Many studies have also shown the efficacy and tolerability of PDE5i for treating ED in patients with cancer and survivors.\textsuperscript{24,25} Importantly, PDE5is are contraindicated in patients taking oral nitrates, because together they can lead to a dangerous decrease in blood pressure.\textsuperscript{26,27}

The timing and dose of PDE5i should be started conservatively, and it should be titrated to maximum dose if needed.\textsuperscript{13} The patient should be monitored periodically for efficacy, side effects, and any significant change in health status. An adequate trial of PDE5i is defined as at least 5 separate occasions at the maximum dose before reporting it as noneffective, unless the reason for fewer trials is an unacceptable side effect. A different PDE5i can be tried after failure of first-line PDE5i therapy.

If the second PDE5i fails, additional interventions can be considered, with referral to a urologist. These options include second-level interventions, such as intrarethral alprostadil suppositories, intracavernous vasoactive drug injection therapy, and vacuum constriction. A third-level and definitive type of intervention, penile prosthesis implantation, can be considered.\textsuperscript{13}

**References**


### Individual Disclosures for the NCCN Survivorship Panel

<table>
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<tr>
<th>Panel Member</th>
<th>Clinical Research Support</th>
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