Current psychiatric distress among patients with breast cancer is common and is linked to worse clinical outcomes. Depressive and anxiety symptoms affect up to 40% of breast cancer patients, and depression is associated with a higher relative risk of mortality in individuals with breast cancer. Psychotropic medications and psychotherapy used to treat depression in patients without carcinoma also are appropriate and effective for breast cancer patients. However, some patients present distinct challenges to standard treatment. For example, growing evidence suggests that some selective serotonin reuptake inhibitors (SSRIs) may reduce the effectiveness of tamoxifen, a chemotherapeutic agent. This article discusses challenges in diagnosing and treating depression in breast cancer patients and reviews evidence supporting appropriate psychiatric care.

Increased vulnerability
In 10% to 30% of women, a breast cancer diagnosis may lead to increased vulnerability to depressive disorders, including adjustment disorders with depressed mood, major depressive disorder (MDD), and mood disorders related to general medical conditions. The risk of developing a depressive disorder is highest in the year after receiving the breast cancer diagnosis. A woman’s risk of developing a depressive disorder may depend on the type of cancer treatment she receives. For example, breast asymmetry is common after breast conserving surgery. Waljee et al found that wom-
Depression and breast cancer

en with breast asymmetry had increased fears of cancer recurrence and more feelings of self-consciousness. More pronounced asymmetry led to a higher incidence of depressive symptoms. However, among 90 patients undergoing bilateral prophylactic mastectomy, the rate of depression had not changed 1 year after the procedure.6 Chemotherapy, particularly at high doses, is a risk factor for depression.4,7,8

Self-blame for developing breast cancer can affect mood. In 2007, Friedman et al9 determined that higher levels of self-blame correlated with higher levels of depression and decreased quality of life. Women often blamed themselves for various reasons, including:
- poor coping skills
- anxiety about their health and treatments
- inability to express emotions
- delays in medical consultation.

Exacerbated symptoms and side effects.
Women with depression often experience increased side effects from cancer treatments, and the subjective experience of these effects—including hot flashes, cognitive impairment, pain, and sexual dysfunction—likely is intensified.4 Somatic symptoms of depression may be exacerbated by cancer treatment side effects or mistaken for effects of the treatment. When somatic symptoms of depression are mis-

<table>
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<tr>
<th>Table 1</th>
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<tr>
<td><strong>Risk factors for psychiatric distress related to breast cancer</strong></td>
</tr>
<tr>
<td>Past psychiatric illness</td>
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<tr>
<td>Family history of psychiatric illness</td>
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<tr>
<td>Younger age (&lt;45 years)</td>
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<td>Having young children</td>
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<td>Limited social support</td>
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<td>Substance use</td>
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<td>Single status</td>
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<td>Pain</td>
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<td>Physical disability</td>
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<tr>
<td>Poor family coherence</td>
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<td>Financial strain</td>
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</table>

**Source:** Adapted from reference 10

Appropriate screening tools
Factors that may increase a breast cancer patient’s risk for developing a psychiatric disorder are listed in Table 1.10 Many depression screening tools are available; below we describe 3 commonly used for patients with breast cancer.

The National Comprehensive Cancer Center Distress Thermometer allows patients to rate their overall distress level over the past week on a scale from 0 to 10, using a visual analogue.12 The Distress Thermometer has been validated for several cancer populations and in different parts of the world. A score of 7 has both good sensitivity and specificity for detecting depression in breast cancer patients. Consider a complete psychiatric evaluation for patients with scores ≥7.13

The Profile of Mood States questionnaire14 is a reliable, valid 65-item questionnaire often used in studies of mood dysregulation and breast cancer. Subscales include depression-dejection, tension-anxiety, anger-hostility, confusion-bewilderment, vigor-activity, and fatigue-inertia. Using a 5-point Likert scale, patients rate their symptoms over the past week. Subscale scores are then added to a total mood disturbance score.14,15

The Hospital Anxiety and Depression Scale (HADS) is a sensitive, reliable 14-
item scale that is commonly used to study depression and anxiety in patients with breast cancer. HADS includes two 7-item subscales—anxiety and depression—and answers are scored on a 4-point Likert scale. Patients are asked to respond quickly and avoid thinking too long about their answers.

**Psychotherapeutic options**

Behavioral therapies can diminish symptoms of depression, according to a review of studies and practice guidelines on managing depression in cancer patients. Group interventions, in particular, can be valuable. Anderson et al found that group cohesion, member connectedness, and more sessions correlated with decreased psychological distress.

**Psychoeducation** aims to provide medical information and discuss cancer’s causes, prognosis, and treatment strategies. Group settings can help improve communication and problem-solving skills. In a randomized controlled trial (RCT) of 203 women with breast cancer, psychoeducational group treatment reduced depression, anger, and fatigue.

**Cognitive-behavioral therapy (CBT)** helps patients identify and restructure negative thoughts and increase positive, adaptive behaviors. Hunter et al noted significant improvement in depressed mood, anxiety, and sleep in 17 women experiencing menopausal symptoms who received group CBT after completing breast cancer treatment. In 1 study, 124 patients with metastatic breast cancer who received 8 weekly sessions of group CBT reported reduced depression and mood disturbance and improved self-esteem compared with a no-therapy control group.

**Supportive-expressive therapy (SET)** is a manual-based therapy that focuses on increasing social support, improving symptom control, and enhancing communication between the patient and treatment team. Affective expression helps lead the therapist to issues that should be addressed. Evidence on the effectiveness of SET for patients with breast cancer is mixed. A study of 357 women with breast cancer who were randomly assigned to 12-week group SET or an educational control condition found no evidence that SET reduced distress. However, a trial of 485 women with advanced breast cancer who were randomly assigned to group SET plus relaxation therapy or relaxation therapy alone showed that SET improved quality of life, including protection against depression.

**Mindfulness-based stress reduction (MBSR)** is a standardized form of meditation and yoga. Clinicians teach patients visualization, breathing exercises, and meditation to help them become aware of the body’s reaction to stress and how to regulate it. In an RCT of 84 female breast cancer survivors, a 6-week MBSR program diminished depressive symptoms, improved physical functioning, and reduced fear of cancer recurrence.

**Evidence for antidepressants**

**SSRIs.** Expert consensus guidelines on treating depression in women recommend an SSRI as a first-line agent. In RCTs, fluoxetine, paroxetine, and sertraline were more effective than placebo in treating depression and related symptoms specifically in women with breast cancer (Table 2, page 46). The interaction between SSRIs and chemotherapy agents is a concern. Tamoxifen decreases the rate of death from breast cancer in hormone receptor positive breast cancers. Endoxifen, a potent anti-estrogen, is an active metabolite of tamoxifen via cytochrome P450 (CYP) 2D6. Goetz et al demonstrated that women with decreased or inhibited metabolism via CYP2D6 had significantly shorter times to breast cancer recurrence, compared with women with extensive CYP2D6 metabolism.

SSRIs can varyingly inhibit CYP2D6. In a prospective trial of 158 breast cancer patients receiving tamoxifen, paroxetine and fluoxetine were found to be strong inhibitors of CYP2D6 and led to low levels of endoxifen. In contrast, weaker inhibi-

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**Clinical Point**

Depressive symptoms can create the impression that a patient is poorly adherent to cancer treatments.
tors, including sertraline and citalopram, led to intermediate levels of endoxifen. In a retrospective cohort study, Kelly et al. demonstrated that women treated with paroxetine, in combination with tamoxifen, had an increased risk of death compared with women treated with other SSRIs or venlafaxine and tamoxifen. They estimated that paroxetine use in women treated with tamoxifen would lead to 1 additional breast cancer death per 20 women within 5 years of discontinuing tamoxifen.

According to American Psychiatric Association practice guidelines for treatment of MDD, depressed breast cancer patients who receive tamoxifen generally should be treated with an antidepressant that has minimal effect on CYP2D6 metabolism, such as citalopram, escitalopram, venlafaxine, or desvenlafaxine.

Serotonin-norepinephrine reuptake inhibitors (SNRIs) may be used to treat depressive disorders. In addition, venlafaxine may be helpful in treating post-mastectomy pain syndrome. Approximately one-half of patients who undergo mastectomy or breast reconstruction may experience a postoperative pain syndrome. The most common symptom is a burning, stabbing pain in the axilla, arm, and chest wall of the affected side. This pain is worsened by movement and is poorly responsive to opioids.

In a 10-week RCT of 13 patients with neuropathic pain after breast cancer treatment, venlafaxine significantly improved pain relief compared with placebo, although the drug did not affect depression or anxiety. In a study of 100 patients given venlafaxine or placebo for 2 weeks starting the night before undergoing partial or radical mastectomy with axillary dissection, those receiving venlafaxine had a significantly lower incidence of pain in the chest wall, arm, and axillary region, and scores of pain with movement were decreased. There was no difference in opioid usage between groups.

Tricyclic antidepressants have been demonstrated to be effective in breast cancer patients. Side effects—notably anticholinergic effects—limit their use as antidepressants, especially when compared with SSRI treatment. In a study that randomly assigned 179 women with breast cancer to paroxetine, 20 to 40 mg/d, or amitriptyline, 75 to 150 mg/d, anticholinergic effects were almost twice as frequent in the amitriptyline group (19%) compared with paroxetine (11%). In a 4-week double-blind, placebo-controlled crossover trial of 15 breast cancer patients, amitriptyline significantly relieved neuropathic pain, but its adverse effects made most patients unwilling to use the medication regularly.

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**Table 2**

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Results</th>
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<tbody>
<tr>
<td>Navari et al, 2008&lt;sup&gt;26&lt;/sup&gt;</td>
<td>193 patients with newly diagnosed early-stage breast cancer were randomized to fluoxetine, 20 mg/d, or placebo for 6 months</td>
<td>Fluoxetine reduced depressive symptoms, improved quality of life, and led to higher completion of adjuvant chemotherapy and/or hormone therapy</td>
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<tr>
<td>Roscoe et al, 2005&lt;sup&gt;27&lt;/sup&gt;</td>
<td>94 women with breast cancer receiving at least 4 cycles of chemotherapy were randomized to paroxetine, 20 mg/d, or placebo</td>
<td>Paroxetine significantly reduced depression during chemotherapy</td>
</tr>
<tr>
<td>Kirnck et al, 2006&lt;sup&gt;28&lt;/sup&gt;</td>
<td>62 women with early-stage breast cancer receiving the chemotherapy agent tamoxifen who reported hot flashes were randomized to sertraline, 50 mg/d, or placebo for 6 weeks</td>
<td>Sertraline was significantly more effective than placebo at reducing hot flashes</td>
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</tbody>
</table>

*Breast cancer patients who receive tamoxifen generally should be treated with an antidepressant that has minimal effect on cytochrome P450 2D6 metabolism, such as citalopram, escitalopram, venlafaxine, or desvenlafaxine

SSRIs: selective serotonin reuptake inhibitors
Depression and breast cancer

Related Resources

Drug Brand Names
- Amitriptyline - Elavil
- Citalopram - Celexa
- Desvenlafaxine - Pristiq
- Escitalopram - Lexapro
- Fluoxetine - Prozac
- Paroxetine - Paxil
- Sertraline - Zoloft
- Tamoxifen - Nolvadex
- Venlafaxine - Effexor

Disclosure
The authors report no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

References

Bottom Line
Women are at risk for depression in all stages of breast cancer. Several forms of psychotherapy can be effective for these patients. Although pharmacotherapy for depression generally is the same for breast cancer patients as for those without carcinoma, be vigilant for factors that influence treatment strategies, such as the possible effect of SSRIs on CYP2D6 metabolism in patients receiving tamoxifen.


