Anxiety and depression in women with breast cancer

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Abstract

Anxiety and depression are the two most prevalent psychiatric presentations among women with breast cancer. If left untreated, anxiety and depression can have serious psychological, medical and health service utilisation consequences. These include reduced likelihood of accepting, tolerating and adhering to recommended treatments, and increased toxicities and severity of medical symptoms that, in turn, can increase healthcare costs and reduce quality of life. Risk factors for anxiety and depression in women with breast cancer include: a past history of anxiety or depressive disorder; younger age at diagnosis (<50 years); poor social support; burdensome somatic symptoms; currently undergoing active cancer treatment; specific drug treatments; and body image distress. Interventions for depression and anxiety in breast cancer have typically comprised a) pharmacological treatments, with citalopram, venlafaxine and mirtazapine being safe antidepressants to treat both anxiety and depression; and b) psychotherapy, with cognitive-behavioural therapy considered the current gold-standard treatment for primary breast cancer, and supportive-expressive approaches more appropriate to women with advanced disease. However, distress continues to be under-screened and under-treated. In order to increase the reach of our services, more tiered and systematic approaches to screening, and a stepped care approach to delivering treatments are required.

Despite improvements in early detection and medical treatment, a diagnosis of breast cancer continues to elicit greater distress for women than any other medical diagnosis, regardless of prognosis.¹ The nature of this distress can range from psychiatric morbidity, such as depression, anxiety, and post-traumatic stress symptoms;³,⁴ relationship and intimacy difficulties;⁵ to quality of life (QOL) impairments, including body image concerns.⁶,⁷ This review focusses on the two most common psychiatric presentations, depression and anxiety, and summarises the resulting impact on QOL. The current evidence base for psychological and pharmacological treatments will be summarised, and future directions highlighted.

Psychiatric morbidity

Although distress and worry in response to a stressful life event is normal (and experienced, to some degree, universally), depression and anxiety are considered problematic when they impair social, emotional, physical and/or occupational functioning.⁸

Prevalence of psychiatric disorder

Using the gold standard for establishing prevalence, a recent epidemiological study of 442 German women with breast cancer found a four week prevalence rate for any mental disorder of 41.6% (95% CI 36.8-46.4%), using the Computerised International Diagnostic Interview-Oncology (CIDI-O).³

Breaking this down by disorder type, the four week prevalence of (a) any mood disorder was 8.7% (95% CI 6.2 - 11.2); (b) any anxiety disorder, 16.8% (95% CI 13.6 - 20.6%); (c) adjustment disorder (with depressed or anxious mood), 14.4% (95% CI 11.0 - 17.7%); and (d) somatoform disorders (including somatisation disorder and hypochondriasis), 8.6% (95% CI 5.8 - 11.3%).³ Mixed
presentations of anxiety and depressive disorders also occurred – while approximately 30% of the German breast cancer sample presented with a single disorder, 8% had two disorders, and 2% had three or more mental disorders.3 This is consistent with the 10.8% mixed syndrome prevalence found in a sample of 1996 women with breast cancer at the Johns Hopkins Oncology Center, while 14.9% were pure anxiety and 2.8% pure depression symptoms.9

While advanced disease is often considered as a risk factor for increased vulnerability to depression and anxiety,10,11 when evaluated using a structured psychiatric interview (DSM-IV), in 303 Australian women with early stage and 227 with advanced breast cancer, rates of psychiatric morbidity were notably equivalent.12 This suggests that the stress of the diagnosis was more relevant than stage of disease.12 Early stage patients had an overall rate of DSM-IV mental disorder of 45%, compared to an overall prevalence of 42% for patients with advanced cancer.12,13 Women presented most commonly with either major depression, in 9.6% (95% CI 6.5 - 13.5%) of early breast cancer patients and 7.0% (95% CI 4.4 - 11.1%) of advanced;12,13 or adjustment disorder with anxious or depressed mood in 24.8% (95% CI 20.0 - 30.0%) of early stage and 24.2% (95% CI 19.1 - 30.2%) of advanced.12,13 Specific anxiety disorders (generalised anxiety disorder, post-traumatic stress disorder, simple phobias, and panic disorder) were less common (ranging from 0.9%-4.3%).12,13

One of the single most prevalent types of anxiety for women is fear of breast cancer recurrence or progression, which is defined as the fear, worry or concern that cancer will come back or progress.14 While experienced by all women to a certain degree, this fear can escalate to clinical levels characterised by preoccupation, worry, rumination or intrusive thoughts; maladaptive coping; impairments to functioning; excessive distress; and difficulties making plans for the future.14 It shares many features of health anxiety (hypochondriasis), including misinterpretation of body sensations as signalling recurrence, reassurance-seeking including excessive health service-utilisation and screening, or cognitive and behavioural avoidance.15 Research further indicates that this worry about future health can have a direct effect on depression, independent of the illness intrusiveness.16

Who is most at risk for anxiety and depression?
A number of risk factors have been established for the diagnosis of mental illness in women with breast cancer, including: (a) personal vulnerability evidenced by a past history of anxiety or depressive disorder, with 30% of people with current depression and anxiety having a past history; (b) younger age (<50 years) at diagnosis; (c) poor social support, represented by relationship difficulties, isolation, alienation and family dysfunction; (d) burdensome somatic symptoms, ranging from breast pain, amputation syndrome, arm pain, difficulty raising the arm, and a variety of non-specific symptoms such as fatigue, insomnia, headache and nausea; (e) currently undergoing active cancer treatment; (f) certain drug treatments such as steroids; and (g) continuing distress at body image change and self-esteem.10,13 Not only is the existential threat associated with the diagnosis of breast cancer troublesome, but the consequences of anti-cancer treatment also contribute substantially to the psychological morbidity associated with this illness.

In addition to the psychological suffering caused, anxiety and depression can impact on health and medical treatment outcomes in numerous ways, including: reduced likelihood of accepting, tolerating and adhering to treatment, increased toxicities and severity of medical symptoms. This in turn can increase healthcare costs and reduce QOL. At the most extreme, untreated anxiety and depression can result in an 18% increased mortality from breast cancer;17 and higher suicide rates.18

Impact of breast cancer on quality of life
Assessment of QOL is seen as an essential component of therapeutic management of cancer patients.19 Research indicates that QOL is globally adversely affected immediately following breast cancer diagnosis and remains impaired over time if untreated.20,21 Prospective and longitudinal Australian data found that two years after diagnosis, women continued to experience significant reductions in general health, physical role, mental health and social functioning compared to women without breast cancer.22

Body image changes are high and cause dissatisfaction and distress in women with breast cancer; these are reflected in perceived loss of femininity, decreased perceived attractiveness as a result of surgery, reluctance to look at oneself naked, feeling embarrassed by use of a prosthesis, and having reduced libido and sexual enjoyment.12,13 In terms of causes of poor body image, empirical evidence
clearly demonstrates that women who have breast conserving therapy have better body image than those who have a mastectomy, and those who have immediate breast reconstruction experience less distress and better psychosocial wellbeing than those who have delayed reconstructive surgery. While the breast loss is a primary source of body image concern, other causes include weight gain or loss from chemotherapy, early menopause and hair loss – with hair loss causing more distress for women with early stage disease, and hot flushes being more prominent in those with advanced disease. One specific body image concern for women with breast cancer is lymphoedema, with rates of arm lymphoedema rising from around 4% in early stage disease to 12% in advanced breast cancer, the latter still within four years of surgery.

Young women with breast cancer (defined as aged 50 or under) may be further impacted by concerns about infertility as a result of their treatment of the cancer. Up to 70% of young breast cancer survivors express a desire for children after treatment and are concerned about the possibility of not having biological children in the future as a result of cancer and its treatment. Research indicates that women with cancer-related infertility may experience negative emotional reactions, enduring distress and strained relationships. Furthermore, recent Australian qualitative data indicate that fertility represents more than child-bearing capacity; it was linked with identity and femininity. Therefore potential fertility loss is a source of considerable distress for patients, irrespective of their desire for future children.

**Treating depression and anxiety in breast cancer**

Interventions for depression and anxiety in breast cancer have typically comprised pharmacological treatments and/or psychotherapy.

**Pharmacological treatment: traps and recommendations**

Pharmacological treatments are a necessary component for the appropriate treatment of women with moderate to severe depression and anxiety. Drug interactions present the main hurdle for the unwary. In particular, several antidepressants that use a metabolic pathway, mediated by cytochrome P450 2D6, in the liver will interfere with the metabolism of tamoxifen to endoxifen, its active metabolite. Among the safe antidepressants to treat both anxiety and depression in women with breast cancer are citalopram, venlafaxine and mirtazapine; ones to avoid include paroxetine, sertraline and fluoxetine.

**Psychotherapy**

Several meta-analytic studies have confirmed irrefutably that anxiety and depression can be successfully treated in women with breast cancer. The largest of these systematic reviews examined over 22,000 patients and recorded medium effect sizes for relief of anxiety and depression from both individual and group therapies, but not couple psychotherapy. Within these modalities of delivering treatment, a wide range of psychotherapies have been trialled, including: cognitive-behavioural therapy (CBT) programs, psychoeducational treatments, relaxation training, problem-solving therapy, mindfulness-based interventions, interpersonal therapy, non-behavioural counselling or psychotherapy, and supportive-expressive therapy. Of these, CBT is considered the current gold-standard treatment for primary breast cancer, while supportive-expressive approaches are more appropriate to women with advanced disease.

CBT is structured in nature, usually comprised of between six and 10 weekly sessions of 60-90 minutes duration, and generally consists of three major components: 1) psycho-education about depression/anxiety in the cancer context, developing a conceptual framework that validates the range of personal symptoms experienced, and outlining responses that typically maintain the disorder; 2) cognitive strategies including cognitive restructuring, distraction, problem solving, and behavioural experiments to test key cognitions, coping skills training and communication; and 3) behavioural procedures, including behaviour activation, exposure, guided imagery/relaxation, and goal setting. For the treatment of major depression, behavioural procedures are typically implemented first; indeed behaviour therapy alone was recently found to yield equivalent benefits to the full cognitive behaviour therapy in a primary care setting, and can be administered by more junior therapists.

In contrast to CBT, supportive expressive therapy was developed specifically for metastatic breast cancer patients as an intensive and comprehensive group program of weekly 90 minute sessions for a 12 month (minimum) period. Unstructured in nature, it was developed within an existential
framework during the 1970s, and was designed to facilitate social support, encourage emotional expression, enhance communication skills, symptom control and deal with existential concerns. Rather than having set weekly topics or strategies, therapists are trained to track emotions that lead to relevant themes and foster group discussion in those areas. An early study controversially found that group supportive-expressive therapy improved the quantity, as well as quality, of life. None of the subsequent supportive-expressive therapy trials replicated this survival benefit and it has since been noted that most participants were married, which is as protective as chemotherapy in cancer care. While demonstrably beneficial for women with metastatic disease, a brief nurse-led 12 session version of the program was trialled in women with primary breast cancer, but its use was unsupported as no effect on distress was found, even among women with high baseline distress.

The benefits of these two therapeutic frameworks for women with breast cancer have also been demonstrated in Australian settings. In a series of group therapy trials, cognitive-existential psychotherapy for women with primary breast cancer demonstrated reduced anxiety and fear of recurrence, cognitive therapy for women with advanced breast cancer reduced depression and improved self-esteem; and supportive-expressive therapy for women with advanced breast cancer reduced depression and improved social functioning. A small effectiveness trial demonstrated that an empirically supported cognitive behaviour group program can be successfully implemented in an applied clinical setting, yielding clinical improvements in cancer-related distress and social support in women with primary breast cancer.

Overall, the evidence base is strong that our psycho-oncologic interventions can ameliorate anxiety and depression; however, not everyone is universally benefitted, and several moderating variables have been identified. These include: 1) the timing and duration of the intervention, with higher effect sizes obtained when offered directly after diagnosis or surgery and longer interventions producing more sustained benefits; 2) the expertise of the therapist, with greater benefits being reported when interventions are delivered by psychologists and 3) baseline level of distress; when participants in trials of individual and group therapy are selected for distress, effect sizes increase to large.

Under recognition and under-treatment of patients in need

Despite this evidence for the efficacy of interventions, many patients in need fail to be recognised by our clinical programs. Distress is normalised as comprehensible and existentially triggered. Clinicians can remain reluctant to probe, for fear of opening a Pandora’s Box; patients may mask what remains a stigmatising problem for many. Efforts have been made to routinise distress screening as one way to redress this challenge, however a tiered approach is further required such that a second level of more specific screening and triage of anxiety and depression, to fully overcome this problem of under recognition.

Even in patients who are screened as distressed, a recent Australian clinical audit indicated only 29% were willing to accept psychological assistance. Barriers to uptake include geography, particularly for those in regional or rural areas, and personal and illness-related barriers, including stigma associated with accessing mental health services. This has led to a recent surge in interest in online psychological interventions, given that 86% of Australians have access to the internet. A number of randomised trials have been recently published in this area, with promising findings across the treatment trajectory for early stage breast cancer. More specifically, the online CBT-based psychological interventions were efficacious in improving: (a) global and physical QOL, cancer-related distress, and anxious preoccupation in Australian women currently going through medical treatment; (b) distress, fear of recurrence, fatigue and self-efficacy during the immediate survivorship period (two to four months after completion of active cancer treatments); and (c) perceived health, coping self-efficacy, emotion regulation, and post-traumatic stress in extended breast cancer survivors. Furthermore, the effect sizes obtained were comparable to those often obtained in face-to-face interventions. While online interventions do not replace traditional therapist-administered options and non-inferiority studies have not been conducted, they are a useful first step in a stepped care framework, and as a treatment option for women where the alternative is no treatment (such as in rural or remote areas).

New directions in the treatment of anxiety and depression in breast cancer

While supportive-expressive therapy and CBT remain the gold-standard treatments of choice, more emphasis in recent times has been placed on the role of perseverative thinking (worry and
Anxiety and depression in women with breast cancer are highly prevalent, but very treatable. If left untreated, there are serious medical and health consequences, which impact on quality of life and healthcare costs. A range of evidence-based pharmacological and psychotherapeutic treatments exist, and new interventions are currently being trialled to reduce the suffering of this population. However, in order to increase the reach of our services, more systematic approaches to screening, and a range of options for delivering treatments (such as through a stepped-care approach) are warranted.

References


