COMMENTARY

Psychosocial/Survivorship Issues in Breast Cancer: Are We Doing Better?

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Abstract

Modern breast cancer treatment offers many women greater prospects of cure or lengthier, good quality survival than was possible in the past. Advances include improved diagnostic and staging procedures, sophisticated onco-plastic surgery, enhanced radiotherapy techniques, and targeted systemic therapies. Much more attention has also been paid to cancer care delivery and access to specialist nurses, counsellors, support groups, and services provided by breast cancer charities. However, there are some concerns that these considerable improvements in treatment delivery and clinical outcomes have not led to similar benefits in the psychosocial, functional, and sexual well-being of women. The impact that non–life threatening, long-term iatrogenic harms of otherwise efficacious anticancer treatments has on patients is often overlooked; this is in part because of the emphasis given to physician-reported safety data in trials and the general exclusion of patient-reported outcomes (PROs). A failure to utilise reliable PRO measures has meant that some problems are underreported, which consequently has hampered much-needed research into ameliorative interventions. Systematic monitoring of quality of life-threatening side effects would permit early implementation of effective interventions and enhance long-term survivorship. Some examples of the pervasive difficulties that continue to affect survivors and evidence that certain interventions might help are provided in this commentary.

The past three decades have seen some extraordinary advances made in breast cancer treatments that offer women greater prospects of cure or lengthier, good-quality survival. Wide publicity is given quite rightly to better diagnostics and improved and less radical surgical techniques, increasing recognition of the need to manage the axilla, specialist oncoplastic surgeons producing more acceptable cosmetic outcomes, less damaging radiotherapy techniques, and new procedures such as intraoperative radiotherapy that reduce treatment time and hospital visits. The explosion in knowledge regarding the genomics and molecular biology of breast cancer has also increased the number of chemotherapeutic options; trials report regularly the progression-free survival (PFS) and overall survival (OS) benefits of the newer systemic cytotoxic, hormone, and targeted therapies.

Unfortunately, nothing comes without cost, and, despite these laudable therapeutic breakthroughs, considerable psychosocial and iatrogenic harms continue to be created by the diagnosis of breast cancer and its treatment. Most of the treatment-related side effects are acute, but some can be long term, impacting quality of life; many women remain plagued by a plethora of physical, functional, emotional, financial, and social challenges. Although responses vary at different stages of the disease trajectory, the impact of these issues preoccupies some women constantly. Importantly, as few patients inhabit complete social vacuums, many of their concerns related to diagnosis and treatment also affect others family members and friends. One positive outcome of psychosocial research exploring these areas of concern and the advocacy demands by women themselves has been the increased awareness of the need to provide access...
to specialist nurses, patient navigators, counselors, and support
groups. In tandem, some influential bodies, such as the Institute
of Medicine (IOM), also made recommendations to promote evi-
dence-based, comprehensive, compassionate, and coordinated
survivorship care plans for all people diagnosed with cancer (1).

Despite all the new treatment options with their resultant
improved clinical outcomes, it is questionable whether or not
these endeavours have led to many comparable, measurable
benefits in patients’ psychosocial, functional, occupational, and
sexual well being. In this commentary, we will outline some of
the primary concerns that women with breast cancer continue
to experience from diagnosis through survivorship and then
review some of the evidenced-based interventions that have
made a difference.

Psychological Morbidity

Much psychosocial research over the past 30 years has focused
on the prevalence of psychological morbidity and has produced
mixed results; some reports suggest that the prevalence of
mood disorders, such as anxiety and depression, is high at diag-
nosis and is unremitting (2), while others have found a decline
over time and little difference from that seen in age-matched
control patients without breast cancer. An interesting recent
meta-analysis of 43 studies compared the prevalence of mood
disorders in cancer survivors with their spouses (17 studies) and
with healthy control patients (26 studies). In a pooled analysis,
the prevalence of depression in 51381 cancer survivors was
11.6%, compared with 10.2% in 217630 healthy control patients.
The prevalence of anxiety was higher: 17.9% in 46964 cancer
survivors, compared with 13.9% in 226467 healthy controls. Of
note, neither the prevalence of depression nor anxiety differed
significantly between survivors and their spouses, demonstrat-
ing the likely wider family support needs (3).

Unfortunately, much of the early research in this area has
been hampered by inappropriate measures and methodology (4)
and some extremely loose use of nomenclature; general distress
is often confused with clinical anxiety states and depressive or
adjustment disorders. This might be in part because of the fact
that most criteria for diagnosing anxiety and adjustment disor-
ders were developed for psychiatrically ill, not physically ill, indi-
viduals. Many women with breast cancer do genuinely confront
continual and real threats that their cancer will recur; conse-
quenty their ‘anxiety’ could be viewed as neither irrational nor
inappropriate. One study of 3300 long-term survivors (two years
postdiagnosis) showed that 47% had a fear of recurrence (5).

Being clear about the precise clinical characteristics of any
psychological morbidity is important when determining the
most appropriate prevention or screening strategies for those
most at-risk and ameliorative interventions. The American
Society of Clinical Oncology (ASCO) has recently published
assessment guidelines (6). A large number of management
options is available. Women with clinical depression or anxiety
need to be assessed properly and offered appropriate antidepress-
sant and anxiolytic therapy. For other forms of more generalized
distress, a variety of interventions are available, including cogni-
tive behavior therapy, aromatherapy and massage, visualization,
expressive therapeutic writing, and art and music therapy. Some
publications of well-conducted randomized controlled trials
(RCTs) have shown that interventions incorporating elements
of mindfulness-based stress reduction can improve mood state
and reduce endocrine-related side effects (7) and that yoga can
improve quality of life, fatigue, and measures of stress cortisol
levels (8).

Iatrogenic Harms and Side Effects of
Anticancer Treatments

Determining healthy long-term adjustment involves more than
assessment of psychological morbidity; the deleterious impact
exerted by many non-life threatening, but quality of life–threat-
ening, iatrogenic harms of otherwise efficacious anticancer
treatments is often overlooked. Five commonly reported prob-
lems—lymphedema, fatigue, vasomotor complaints, sexual dys-
function, and cognitive impairment—are considered below.

Lymphedema

Although there have been substantial improvements made
within breast cancer surgery, with oncoplastics specialists able to
offer procedures that are less radical and improve cosmesis, man-
agement of the axilla remains problematic. Some women feel
that the aftermath of axillary surgery is worse than the surgery to
the breast, creating substantial arm morbidity with lymphedema,
pain, loss of sensation and mobility. Lymphedema in particular
remains a problem for many women who have to undergo axil-
lary treatment. A systematic review of 72 studies showed that
the overall risk of lymphedema is 17% (9). Those factors influenc-
ing risk included more extensive surgery, the number of lymph
nodes removed, and obesity. There are at least 18 RCTs compar-
ing axillary lymph node dissection with sentinel node biopsy that
show the risk of lymphedema to be 19.9% and 5.6%, respectively.
Sentinel node biopsy has been shown to reduce the amount of
axillary surgery required without necessarily compromising sur-
vival. It also improves quality of life and reduces arm morbidity
generally (10). As systemic therapy has improved outcomes for
patients substantially, some doubt whether or not all women with
early breast cancer and minimal nodal involvement really need
to have axillary surgery at all, so large trials are required to dem-
onstrate the safety of this approach. We do know that efforts to
reduce arm morbidity and, importantly, to prevent lymphedema
through optimal surgery are absolutely vital, as few interventions
help after its occurrence. The trials comparing compression ther-
aphy with complex decongestive therapy (massage, exercise, and
skin care) are sadly equivocal (11).

Fatigue

Fatigue has probably replaced nausea and vomiting as the big-
gest post-treatment problem; it is usually acute, but around 30%
of women experience enervating fatigue that may continue for
many years. The etiology of fatigue is complex; there is certainly a
psychological component, as it contributes to and/or is associated
with reduced motivation, depression, concentration, impaired
activities of daily living, and poor overall health-related qual-
ity of life (12). However, proinflammatory cytokines have been
cited as the most likely underlying biological mechanism (13).
Interventions are very important to initiate early. Although seem-
ingly counter-intuitive, rest is clearly the wrong option and exer-
cise has been shown in many studies to improve not only fatigue
but mood state also. An updated Cochrane review of 56 studies,
28 of which were in breast cancer, showed the benefits particu-
larly of aerobic exercise, but not of resistance training (14). Some
patients find it quite difficult to engage with exercise programs
post-treatment, especially if they have not done this regularly
prior to breast cancer; so they need considerable encouragement
from caregivers, family, and friends or help from a motivational
counselor (15). The more reluctant might be helped by yoga,
acupuncture, and other mindfulness-based programs, although the evidence base for these approaches is less compelling. ASCO recently published guidelines for the screening, assessment, and management of fatigue in adult survivors of cancer generally (16), which could be of benefit to women with breast cancer if implemented as part of their comprehensive cancer care.

**Hormone Therapy**

There are now many data demonstrating the benefits in estrogen receptor–positive women of extending adjuvant therapy to five or even 10 years (17). However, it is unfortunate that many of the women being treated with these drugs will derive no benefit whatever and only experience the iatrogenic harms. Side effects such as vasomotor complaints, vaginal dryness, loss of libido, and arthralgia are more than just a minor inconvenience and can lead to treatment discontinuation and suboptimal adherence (18). Patient self-reports compared with physician reports show that many endocrine-related side effects go under-recognized, underreported, and undertreated (19, 20).

**Vasomotor Complaints**

Vasomotor complaints include hot flashes, cold sweats, and night sweats that lead to sleep difficulties, which themselves may contribute to fatigue and poor concentration. Estimates vary according to the method of assessment employed, and if problems are physician or patient reported, but approximately a third of women experience severe vasomotor side effects attributable to selective estrogen receptor modulators or aromatase inhibitors (AIs) (21). Although not life threatening, these unpleasant consequences of treatment have a profound deleterious impact on overall sense of well being and can affect adherence to oral therapies. Women do need effective nonhormonal treatments to ameliorate vaso-motor side effects. A Cochrane review (22) looked at interventions that might help. The authors identified 10 pharmacological RCTs that included clonidine, gabapentin, serotonin plus or minus norepinephrine reuptake inhibitors such as venlafaxine, paroxetine, sertraline and fluoxetine. All showed some activity in reducing frequency and severity of hot flashes, but there are some contraindications limiting their use in all women. Six nonpharmacological studies were reviewed; these included some reasonable interventions, such as relaxation therapy and acupuncture, together with other more dubious ones such as homeopathy and magnetic devices. Unfortunately, all six studies had many methodological limitations; only relaxation therapy reduced both the frequency and the severity of hot flashes. More recent research has shown the benefits of behavioral approaches such as cognitive behavior therapy (CBT). A carefully conducted RCT of usual care or usual care plus group CBT (90 minute weekly sessions for six weeks) in women with problematic hot flashes and night sweats showed statistically significant reductions in problems nine weeks after randomization, which were maintained at 26 weeks (23). The authors point out that as this safe type of behavioral intervention also has the additional benefits of improving mood state, sleep, and overall quality of life, it seems useful to incorporate into breast cancer survivorship programs and could be implemented by appropriately trained nurses.

**Sexual Problems**

There are many reports of the sexual difficulties created by breast cancer and its treatment. Vaginal dryness, discharge, and dyspareunia combined with a loss of libido exert a negative impact upon patients and their partners. A study of over 1000 Australian women showed that 70% of breast cancer survivors experience sexual problems in the two years following diagnosis (24). Interestingly less than 80% of these patients claimed to have had a satisfying sex life prior to diagnosis. Those taking AIs were 50% more likely to report problems than those taking tamoxifen or not having any endocrine therapy. Seventy-seven percent of the sample had hot flashes and night sweats, which were linked to reporting of sexual difficulties. Interventions to help loss of libido, vaginal dryness, and dyspareunia are likely to be multifactorial. Studies suggest that moisturizers are probably better than lubricants for vaginal dryness, and combinations of moisturizers with pelvic floor exercises and relaxation training have been shown to be useful (25).

A more general point worth raising regarding the side-effects of otherwise effective treatments for breast cancer concerns the reliance on clinician-reported safety data rather than information collected via patient-reported outcome measures in clinical trials. This has led to poor recognition of many of the difficulties some women experience, which in turn has hampered research into much-needed ameliorative interventions.

**Cognitive Problems**

Many women treated with chemotherapy experience memory and attention difficulties, often described as “chemo-brain” or “chemo-fog.” Wide variance exists in the proportions of women reporting problems, partly explained by differences in the neuropsychological tests employed in studies, and the sundry reference data and performance cutoffs used when classifying test results (26). Although chemotherapy may be a key contributor to reported dysfunction, it is not the sole cause of “chemo brain,” as a third of women perform poorly on cognitive tasks following surgery but prior to starting adjuvant therapies (27). In addition, some studies suggest that endocrine therapies play a role (28), although a double-blind RCT of anastrozole vs placebo (IBIS II) in postmenopausal women with a high risk of breast cancer found no differences between the groups for either self-reported problems or for any objective cognitive assessment (29). A recent prospective study of 189 women who had completed primary breast cancer treatments but had not started endocrine therapy found associations between subjective cognitive complaints and performance on some neuropsychological tests, particularly for those who had received both chemotherapy and radiotherapy (30).

The profile emerging from the plethora of studies is one of a mild cognitive impairment affecting learning and memory, processing speed and executive function (31). The mechanisms underlying the phenomenon are not clear, but suggestions include stress and coping styles (32), direct neurotoxic injury, telomere shortening, oxidative stress, cytokine dysregulation, estrogen-mediated effects, and genetic polymorphisms (33). Proinflammatory cytokines can be used as markers for cognitive function in neurological disease, and recent literature suggests that elevated levels of peripheral proinflammatory cytokines may be related to cognitive problems in cancer patients (34). Additionally, decreased estrogen levels may serve as a link between multiple mechanisms potentiating the effects, particularly in those women who experience an acute menopause following treatment.

Imaging studies have documented structural changes to the brain after completion of chemotherapy (35); again, however, some structural differences may have already been present before starting chemotherapy (36).
The literature to date shows that in order to get a true understanding of the extent of this phenomenon, a multifaceted approach is required. Well-designed prospective studies are needed. These would ideally assess women prior to breast surgery, use matched control groups, incorporate imaging and biological measures and records of all the additional "side effects" of treatments that could contribute to poor cognitive functioning, for example, anxiety, pain, fatigue, and sleep disturbance. Having a good preillness measure of how someone is functioning, the work they do, and their family commitments and ability to cope with changes in their life is also important in order to measure the real life impact on the patient.

Communication

Communication affects adjustment to the diagnosis and patient decision-making about treatment. The increasing complexity of our understanding about breast cancer and the number of therapeutic options now available has made discussions between patients and doctors very much more difficult. Breast cancer is no longer a simple disease to explain, and patients already experiencing emotional turmoil enter a strange new world of esoteric language and concepts. Helping patients navigate their way through all this to ensure that they can genuinely provide educated and informed consent to treatment plans demands excellent communication skills from the healthcare professionals involved with breast cancer care. There are also some good web-based information sources available on YouTube, together with DVDs, leaflets and booklets describing treatment options, outcomes with and without treatment, uncertainties, and clinical trial enrollment. A Cochrane review of 55 trials of 23 different screening/treatment decision support tools revealed that women who accessed them showed increased knowledge, more accurate risk perceptions, and greater comfort with their decisions and engaged in greater participation in decision-making (37).

An issue worthy of more research concerns the gross disparities that exist in survival outcomes among patients in groups with different socioeconomic statuses (SESs). Not only do those in lower SES groups have less time with healthcare professionals, but they are also not confident when asking for explanations about care plans and are unlikely to access online informational sources or support services shown to help others in higher SES groupings.

Metastatic Breast Cancer

There has been far less psychosocial research in metastatic breast cancer (MBC) compared with that in early disease. Women worldwide with advanced breast cancer attest to the sense of abandonment and neglect that they frequently feel (38). In a US study of expressive therapeutic writing in 176 women with MBC (39), 48% reported difficulty talking to others, often denying the severity of their illness or prognosis to close friends and relatives. Most had experienced shock, isolation, and a loss of control. As far as the need for further treatment was concerned, hair loss caused many “devastation.” Most activities of daily living changed substantially. Their primary physical problems of fatigue and pain led to them cancel activities, which caused guilt. For some, the inability to work was a major challenge, and frequent medical appointments produced emotional strain. Almost all found the impact on their families distressing. Clearly, much more work needs to be done to help women unfortunate enough to develop metastatic disease.

Conclusions

It is debatable as to whether or not the provision of psychosocial care has kept pace with advances in breast cancer treatment. There is, however, a growing consensus that psychosocial care should be well integrated into routine cancer care with an emphasis on changing from how long to how well patients live (40). There are good suggestions as to how this might be achieved in the developed world, where resources are more likely to be available, but even in these communities ensuring access for different ethnic and minority groups needs more effort (40). Although worldwide, the provision and receipt of psychosocial care remains patchy, three developments in the past decade do enhance the likelihood that it will eventually become a component of comprehensive cancer care: 1) we are much better able to define standards; 2) many organizations have developed and are updating useful clinical practice guidelines; and 3) there has also been some excellent work in the development and implementation of measurable quality indicators.

So are we getting better at enhancing survivorship in breast cancer? The answer is probably yes, but improvements have been mainly seen in early breast cancer, not metastatic breast cancer, which needs addressing. Obviously, it remains important that there is global access to the best treatments and that thought is also given to the preferred routes of administration. We need to have systematic monitoring of side effects of treatment to permit early implementation of evidence-based interventions that might include more integrative oncology, utilizing, where appropriate, nonpharmacological modalities. There is still work to be done ensuring that all healthcare professionals have the communication skills required so that they are capable of providing women with good, consistent, timely, accurate, and understandable information.

Women’s reactions to breast cancer and its treatment vary enormously irrespective of culture or class divides. For some, the diagnosis is a catastrophe, irreparably threatening their physical, functional, social, psychological, sexual, and occupational well being. For others, it represents yet one more of life’s hurdles to overcome together with other social, educational, and financial inequities they face.

Consequently, just as with the exciting advent of personalized and targeted medicine, we need similar endeavors producing more individualized psychosocial care; communication should be flexible, adapted to the varying needs of individuals; appropriate screening should enable resources—counseling, relaxation therapy, yoga, exercise, or mindfulness training—to be focused on those at greatest risk of the unremitting psychosocial dysfunction that compromises healthy survivorship. Spreading scarce supportive services thinly for all irrespective of their need or risk of poor adjustment makes as much sense as administering hormone treatment or trastuzumab without information about receptor status.

References


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