Psycho-oncology and Quality of Life

The subjective experience of breast cancer across the disease trajectory

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Introduction

Breast cancer (BC) remains the most common cancer in women worldwide and the chief cause of neoplastic deaths in women (1). The subjective experience of BC is a particular concern since it affects women of all ages, involves complex care, and affects a body part with great significance to women and their partners (2).

With the decline in mortality rate for BC in the developed world, more women live with the sequelae of treatment, making it crucial to evaluate how cancer impacts on these women’s life. Principle interventions include surgery, radiotherapy, chemotherapy, and endocrine therapy, each of which may have short or long term side effects (3, 4). Although the majority of patients today in the developed world are diagnosed with early-stage localized BC disease, and can expect a life span that is nearly equivalent to women who have never been diagnosed with this illness (5), many women in poorer countries are diagnosed at later stages due to lack of awareness and reduced access to health care (2). For these patients BC is a chronic illness requiring continued biomedical or supportive care interventions.

What does it feel like to be diagnosed and treated for breast cancer? This is the question that measures of health related quality of life (HRQOL) try to answer. Since the first two studies addressed this topic with patients struggling with advanced disease nearly forty years ago (6, 7), several reliable and validated patient self-reported questionnaires have been developed to assess the subjective experience of cancer patients. These questionnaires can tell us what cannot be seen through objective examinations in the laboratory. They shed light on the impact of the disease and treatment across several domains ranging from their symptoms and physical functioning, to cognitive and psychosocial concerns (8). The concepts addressed by these measures are referred to as patient-reported outcomes (PROs) because the data collected are reported directly by the patient (9); in addition to HRQOL, PROs include satisfaction with care and perception of care needs, which target the subjective experience with health care interventions and support services (10).

The goal of this paper is to synthesize what is currently known about patients’ subjective experience of BC and its treatment. We begin by clarifying the concepts of quality of life and health-related quality of life and of care needs; then we describe the roles and the challenges of their assessment in oncology. Assessing HRQOL and care needs with a rigorous methodology allows for describing BC subjective experience and then, planning, monitoring and evaluating supportive care interventions and services, which ultimately target patients’ HRQOL. Next, we review the latest information that these tools have taught on the subjective
impact of diagnosis, the different BC treatments, the surveillance phase and, finally, look at supportive care interventions. Figure 1 pictures the conceptual framework of these subjective outcomes.

Measuring the subjective experience of breast cancer

What do we mean by Quality of Life and Health-Related Quality of Life?

Quality of life is a broad term referring to the general welfare of individuals or societies (11, 12). It will be defined differently from the point of view of specific disciplines such as education, governance, human rights, economics, or health. According to the World Health Organization quality of life refers to an individual’s perception of his or her situation in life across physical, emotional, social, and cognitive domains as well as personal values, goals, and existential concerns (13). The term health related quality of life is more specific since it focuses on patient perception of his or her state in the face of disease and treatment. It may span many of the same domains depending on the evaluation tool that is used. In assessing HRQOL, the impact of mastectomy will not only be considered as far as arm function and prevention of lymphedema, but also perception of body image, and social role. In the same way, the impact of the disease and treatment on couple relationship will extend beyond sexual function alone. HRQOL is typically assessed several times along the cancer trajectory, thereby allowing us to better understand the patient’s changing difficulties from diagnosis, through treatment and on to survivorship.

Presently the most widely used measures of HRQOL in cancer research (14) are the EORTC QLQ-30 (15), developed by the European Organization for Research and Treatment for Cancer, with its breast cancer module, QLQ-BR23 (16) and the FACT-G, the Functional Assessment of Cancer Therapy-General (17), along with the FACT-B, specific to BC (18). Other HRQOL instruments that may be used in the BC setting may address more specific issues such as depression, anxiety, fatigue, or are aimed at specific populations, such as the EORTC elderly module (19) (For a comprehensive list, see references 5, 20).

Assessment of care needs

Another approach to appraise and improve the HRQOL of cancer patients from diagnosis onwards is to evaluate care needs. This refers to the gap between what the patient
needs and what care and services are actually received (21). Assessment is not limited to how physical functioning affects a person’s HRQOL, but attempts to identify which issues are of actual concern to them such as their information needs (22). Patients rate items not only by their severity but also whether a need is met or remains unsatisfied, and to what degree. For example, someone may rate their difficulty with physical effort as being severe, but only when assessing unmet needs do we learn they do not need help in this area because they have already found assistance. This allows providers a better picture of which aspects of care require improvement and where resources should be allocated (23). In contrast, a physician focusing exclusively on physical symptoms and function will too often miss the issues that most concern his or her patient (24). Support care needs surveys may also help give voice to problems patients refrain from mentioning because they believe these are inevitable in cancer or because they are outside the symptoms physicians generally address (25).

The Support Care Needs Survey (SNCS) is a frequently administered tool used to evaluate unmet care needs targeting five domains: physical and daily living, psychological, sexuality, health system and information, patient care and support (24, 26). (For an extensive list of other less common surveys, see reference 25).

These outcome assessments in cancer—the subjective perception of HRQOL or of care needs—allow us to better understand the impact that disease and treatment have on patients so as to design, monitor and improve the care that is provided.

**Patient-reported outcomes (PROs) assessment—applications and challenges**

PROs assessment is relevant in the setting of epidemiological and cost-effectiveness, clinical research as well as more directly at the patient’s bedside.

In clinical research protocols, it contributes to the description of symptoms and difficulties and to the selection of optimal therapy between treatment arms (3). By describing the impact of various types of cancer and their treatments on patients’ global quality of life, PROs assessments provide data that may reveal which symptoms and difficulties encountered by patients require targeted interventions.

Still in the clinical research setting, PRO measures add prognostic value to biomedical indicators such as tumor progression (27, 28). PROs may then be considered for stratification purposes in future trials. Further studies are needed to determine whether interventions that improve PROs also increase survival and to identify explanatory mechanisms through which PROs relate to survival. In BC, most studies showed that baseline HRQOL data predicted survival in advanced BC patients but not in the early stage of disease (28, 29). Various
interpretations have been given, including direct causal link between HRQOL data, being either markers of patient’s behavior, or of personality or coping style, that may affect the disease process, and survival but another plausible explanation is that the data of HRQOL would reflect a perception of the patient on its own health, whose predictive value would be superior to the traditional factors used by clinicians (27, 28).

In the consultation, PRO measures may be used to improve communication between a patient and the health care professionals (30). These consist of screening tools or clinical assessment checklists to identify or monitor the impact of the disease and treatment on patients. In this context, the PRO data gathered in the comparison of therapies may be used in the clinician-patient interaction to estimate the benefits and inconveniences of each option with the patient. The content of the assessment instruments may then encompass issues beyond HRQOL assessment components that patients find important, want to be addressed by their clinicians (31). These issues may comprise information about treatments (options, benefits, and side effects) and care coordination (24).

Whereas the value of patients’ perspective is widely recognized across application contexts (32), the measurement of PROs and interpretation of PRO data remain challenging. Data collection itself requires time and effort both on the part of patients and health care providers. It can be tiring for someone who is ill to complete these questionnaires. The scoring and interpretation of the data requires training that not all health care professionals attain. This is compounded when multiple questionnaires are used requiring more sophisticated statistical analysis. The development of computer-adapted tests is designed to improve the precision of measurement while minimizing patients’ burden (32).

Furthermore, most of these tools were developed for use in clinical research, in order to assess differences between groups of patients in response to new interventions or drugs (3). Statistical and clinical significance does not have the same meaning (33); a statistically significant difference in a PRO questionnaire scores may not translate in perceived change in patients. Additional work has to be performed to establish the interpretability of differences in PRO questionnaire scores so as to anchor “the improvement in the life that a cancer patient may feel significant” enough to potentially prompt a request for a change in treatment (8, 33).

In addition, certain items on PRO instruments may not apply across the whole cancer trajectory. For example an item may be relevant during treatment (assessing the toxic effects of chemotherapy, for example) but not in survivorship (3). Needs change too, as symptoms, functional status, or attitudes change. For example, the need for information may not be
expressed at diagnosis, but only later, once the patient has integrated the reality having BC (2).

Repeated evaluation assures health care professionals can gain a better sense of the patient’s evolving concerns. However, a phenomenon challenges the interpretation of repeated assessment: the response shift (34). It corresponds to an adaptation response resulting from a change in an individual’s standards, values and/or conceptualization. A change in the individual’s health over time seems to lead to a change in how that individual views his/her HRQOL. Further research needs to be undertaken to quantify the magnitude of this shift and its importance in interpreting the clinical significance of changes in HRQOL scores (8).

**What do studies tell us about the breast cancer experience?**

PRO measures have been used with patients diagnosed and treated for cancer across the trajectory of the illness, and for varying types and stages of the disease. This includes reports just after diagnosis; in women with early stage BC or advanced local disease; in metastatic disease at diagnosis; in remission after a course of primary treatment; at first recurrence; palliative care; long-term survivorship (5). With the advent of genetic testing, women found to be at high risk for cancer have their own HRQOL issues, for example, the difficult choices they face regarding prophylactic interventions (35).

We will now review some of what we have learned about the concerns of women diagnosed and treated for BC through the administration of HRQOL questionnaires and care needs surveys.

**The impact of a diagnosis of breast cancer**

For most women, learning that they have BC is a devastating experience. BC forces a confrontation with death and with fears of suffering, pain, mutilation, and loss of femininity and sexuality. The newly diagnosed BC patient may feel anxiety, depression, and anger, with prevalence of psychological distress at up to 50% at diagnosis and in the primary treatment phase (36-38). Specifically, depression and anxiety were assessed at 33% at diagnosis and 45% at recurrence (39). In a large cohort of BC women, Hopwood (40) highlighted at baseline a prevalence rate of borderline and clinical cases of anxiety and depression of 34.9%.
Even when prognosis is excellent, as in the case of ductal carcinoma in situ (DCIS), women are confronted with the same existential threat, perhaps because treatment is similar to that of invasive BC, which leads to an inaccurate perception of risk (41).

Depression reduces HRQOL and adherence to treatment, increases the length of hospital stays, and difficulty in understanding information (42). Interventions targeted at reducing psychological distress may lead to better health outcomes (43) and decrease in depression symptoms has been associated to longer survival in advanced BC (44).

The patient’s satisfaction with information and communication with her doctor will be particularly important at this time in selecting the treatment plan. Although HRQOL measures point to distress as the major impact on wellbeing at this time, studies show, among various cancer types (45) and in BC patients specifically (46), that the greatest need reported is foremost the need for information followed closely by psychological needs, the latter compounded by financial difficulties. Another study with a large sample representing different cancer types puts psychological concerns before informational needs (47).

No matter which treatment is chosen, or what the outcome, patients are more satisfied when they perceive that they have participated in the decision making process (48). However, how much the patient desires to be part of this process varies and it is having participated as much as one wishes rather than participation per se that leads to satisfaction with outcome (49). This further underlines the importance of discerning the needs of the individual patient.

The impact of cancer treatments

Breast cancer treatments often have toxic side effects that appear to be worse than the disease itself in early stages of the illness. Multimodal treatment is common, such as surgery followed by radiotherapy and systemic therapy. Depending on the choice of treatment, the patient may experience nausea, fatigue, loss of hair, mouth sores, body dysfunction, premature menopause, breast removal and alteration of body image, including the constant threat of mortality and psychological distress, leading to reduced HRQOL (2, 50). Supportive care needs during treatment are widespread and variable, among various cancer types including BC, the highest in the domains of physical and daily living, and psychological needs (47, 51, 52). Receiving a combination of treatments is associated to the expression of greater needs (47).

Surgery
Initial treatment for BC is usually surgery, which can be more or less invasive, from lumpectomy to total mastectomy including auxiliary lymph node dissection depending on tumor size, location, expected cosmetic outcome, prior radiation or contraindication to radiation, and patient preference (2, 8).

Breast removal involves the loss of a feminine sexual organ, loss of sensation, and an altered body image, which may persist even with breast reconstruction. However, because of the precision of magnetic resonance imaging scans used for local staging, more women may be requesting ipsilateral mastectomy with contralateral prophylactic mastectomy than before (53).

Women who receive breast conserving therapy (BCT) report fewer difficulties with body image, less numbness, and less pain or needling compared to those who have had mastectomy alone or mastectomy followed with breast reconstruction (54). However, BCT is a complex procedure that does not always lead to improved HRQOL (54, 55).

Women who have undergone aggressive mastectomies, with or without adjuvant chemotherapy, continue to experience muscle stiffness, pain, and decreased physical functioning compared with women who have had a lumpectomy only, however, differences in HRQOL between patients tend to wane over time (8, 56-58).

Breast reconstruction is discussed in about a third of the patients, mainly with younger women with a higher level of education (55). This procedure involves specific features in terms of nature and timing, consideration of breast symmetry and nipple-reconstruction; these need to be discussed with the women. Women generally prefer an immediate rather than delayed breast reconstruction (59).

Comparing breast conserving surgery with mastectomy with or without breast reconstruction, both mastectomy groups reported more physical symptoms, with a higher impact on sexual life in women receiving breast reconstruction (54). With regard to the type of breast reconstruction, transverse rectus abdominis myocutaneous flap (TRAM) or implant, Clough (60) evidenced a decrease in cosmetic result over five years in women receiving implant.

Specific needs after surgery will be associated to the patient’s symptoms and functional status, body image issues and sexuality such as help needed with daily living, information, and psychological domains (52). Prevalence and level of needs will depend not only on the extent of the surgical treatment, but on the adjuvant treatment that generally follows.
Radiotherapy

Breast conserving surgery is commonly followed by whole or partial breast irradiation. Side effects include fatigue, arm, shoulder and breast pain, edema, and skin reactions (60). Irradiation also increases the risk for developing lymphedema in the years after treatment, although the risk is reduced through improved surgical interventions such as the use of sentinel node biopsy, and the irradiation of the breast only (2). Women with the highest levels of anxiety and depression at the start of treatment risk subsequent psychological distress, although different patterns of change over time are associated to age and education and baseline distress (40). Patients’ needs at this time will be associated to difficulties due to fatigue, pain, daily living, and psychological needs related to anxiety.

Systemic Treatment

Systemic treatments comprise chemotherapy and endocrine therapy, which are adjuvant treatments that reduce the risk of recurrence (2). These treatments may elicit acute and persistent side effects, which may affect patients’ perceived functioning and HRQOL.

Most common side effects associated to chemotherapy include fatigue, damage to mucosal linings throughout the body, weight gain, and loss or thinning of hair which may lead to feeling unattractive, self consciousness, and the loss of sexual desire, which are due to the changes wrought upon the body’s hormonal levels (62). Nausea and vomiting is common with certain chemotherapy agents and dosage used (63). Of particular worry to young women is that premenopausal symptoms may become permanent (64). Memory and concentration deficits have also been reported although the observed relationship between subjective cognitive dysfunction and anxiety or depression suggests it is more indicative of emotional distress than objective cognitive disorder (65).

Endocrine therapy refers to hormonal drugs that may be used alone or together with chemotherapy. Symptoms of endocrine treatment comprise mainly menopausal or gynaecological symptoms, arthralgia, and headaches (64). These differ according to the prescribed treatment, although hot flushes, fatigue, nausea, vasomotor, and gynecological symptoms are common. Examples of these drugs are tamoxifen and raloxifene. A newer group of drugs are aromatase inhibitors, such as anastrozole, which may induce fewer cold sweats and vaginal discharge, yet more vaginal dryness, painful intercourse, and loss of sexual interest (65). They may also have long term effects on the heart and bone density (64).

Newer therapy (eg, taxanes, granulocyte colony-stimulating factor) may induce pain syndromes whereas molecularly targeted agents (e.g., trastuzumab) are less toxic. In a
longitudinal case-control design study, in women with stage II or III BC, taxane-based adjuvant chemotherapy increased emotional distress and induced higher rates of probable clinical depression; in addition women treated with taxanes reported twice as much time to recover than those who did not receive taxanes (67).

Systemic treatments affect psychosocial function, due to the loss of sexual desire, fatigue, feeling unattractive, opening the way to anxiety and depression. Assessment of HRQOL before and after treatment is essential for choosing optimal care, insuring adherence, and can also aid in disentangling symptoms and distress as a result of treatment from other stressors. Patient needs revolve around relief from the symptoms related to the drugs prescribed, and to psychological distress. Although many women adjust well to cancer, unmet needs may remain present years after treatment is concluded.

Regards of the type of initial treatment, a year later there seems to be marked improvement in HRQOL for most women, although those who were treated with adjuvant chemotherapy reported higher levels of anxiety and depression, and more enduring symptoms (40, 68).

**Surveillance**

A year after treatment is completed the HRQOL of BC patients rejoins those of the general population, a measure of the resilience of survivors (69, 70). This holds true also for patients after treatment of recurrence even though they experience poorer functioning compared to those first diagnosed (70).

Long-term HRQOL has been studied in a recent large French registry-based controlled study showing clinically significant higher level of fatigue, lower physical and role functioning in BC survivors compared to controls; however, these differences decreased with time and 15-year cancer survivors were generally not different from controls (71). These results are in line with similar studies in other countries (72, 73).

However, after BC treatment many women are left with difficulties in several areas such as pain, fatigue, sexual dysfunction, and psychological distress. Sexual difficulties may persist, especially in younger women where hormone deficiency or alteration of body image may lead to decreased sexual satisfaction, which may induce relational tensions or communication problems with their partners (74, 75). Nonetheless, BC is not associated with a significantly higher divorce rate (76).

The end of primary treatment means the loss of the supportive care environment provided during treatment and worries of recurrence surface. Endocrine treatment that may be
prescribed for 5 years provides a sense of security; however the accompanying side effects (e.g., joint pain) may have the dangerous result of treatment discontinuation (77).

Although over 70% of all types of cancer survivors report positive emotional changes in their lives as a result of their illness (69) others develop constant anxiety about their health, and find it difficult to plan for the future (2). Having high physical and psychological needs at end of treatment predicted persistent needs six months later (52). While 30% of patients reported no or few needs six months after the end of treatment, there were also another 20% who reported little improvement in their lives. In addition, hormone therapy is associated with greater unmet needs during survivorship (78). The most frequently reported unmet need is psychological, and recurrence is the most common concern (78).

Given that mental HRQOL is more susceptible to impairment in BC patients compared to other cancer patients, studying predictors of long term mental HRQOL in BC may be particularly relevant. One recent study highlighted that negative affects, younger age, chemotherapy and lower social support were risk factors for lower long-term mental health and these predictors were stronger after BC experience than after any other stressful life event (79). This underlines factors that may help screen for BC survivors in need of psychosocial intervention.

A third of women with recurring cancer or who are diagnosed with advanced BC and receive treatment for several years report globally low HRQOL with physical and social role difficulties (22). Fatigue is common in about half of all cases and while physical difficulties are related to daily living needs, the highest unmet needs remain in the psychological and health information domains. However, the psychological concerns of these women are different from those in remission. These women know there is no cure; instead of recurrence they worry about how to best care for themselves and their loved ones (22). Evaluation of their HRQOL and unmet needs will insure that these women gain access to information and to supportive care services.

**Supportive care**

The primary goal of supportive care is to preserve or enhance the patient’s HRQOL. Supportive care includes biomedical or non biomedical interventions that complement specific antitumor therapies with curative intent. These interventions help the patient cope with all aspects of the cancer experience throughout the course of the disease. This may include help with pain management and physical or functional difficulties, alleviating distress
with drugs or psychosocial interventions, and help with practical necessities such as transportation, prosthetics, and wigs (56). Supportive care interventions which are based on a patient-centered care approach are essentially evaluated in terms of satisfaction with care (79).

Medications to treat anxiety or depression must be prescribed judiciously, as selective serotonin reuptake inhibitors (SSRI) anti-depressants may interfere with hormonal treatments such as tamoxifen (81). In the adjuvant treatment and metastatic disease setting, some drugs (such as erythropoeitin) target cognitive dysfunction and transfusion rates, while other treatments have been tested for alleviating menopausal symptoms (such as phytoestrogens and magnets), but with inconsistent results (see 57 for a review of clinical trials). Fatigue and nausea may be eased with exercise (82, 83).

In the palliative setting, biphosphonates for bone metastases may improve HRQOL and reduce pain; however, patients’ satisfaction with different biphosphonates administration modes (oral vs intravenous) may vary such that, for oral forms, patients expressed dissatisfaction with the constraints related to taking the tablets (84).

Psychosocial interventions such as support groups, individual therapy, psycho-educational programs, relaxation sessions, and coping-skills training have been shown to improve the HRQOL of BC patients, reduce distress, and improve body image (2, 85, 86). Interventions that reduce anxiety and depression appear to have both direct and indirect effects on patient health, and may even reduce recurrence and extend survival, although this claim is controversial (43).

**Conclusion**

In this chapter we reviewed the conceptual and methodological underpinnings of assessing the subjective experience of patients affected by BC. We then journeyed from a diagnosis of BC through the different treatments and into surveillance to review what is known about the impact of the disease on HRQOL. Diagnosis and treatment of BC is a devastating experience for most women. Besides having to face their own mortality, most BC patients undergo potent treatments that create physical and psychosocial difficulties that reduce HRQOL and lead to specific needs.

This updated literature overview highlighted areas that deserve further research attention. First, there is a need to improve understanding of symptoms related to BC treatment, especially to the new treatments such as targeted (biological) therapies. In
addition, the identification of symptom profiles that may have common biological pathways may lead to new management strategies (87). In particular, cognitive deficits reported by BC patients may be related to other symptoms like sleep problems, fatigue, depression and it is important to elucidate the extent to which this is due to treatment, to the general effects of cancer, or to personal characteristics. Second, psychosocial interventions have proved beneficial in the adjuvant setting; however, it is not clear whether these are currently used in clinical practice (57). Barriers to implement these interventions may be related to insufficient dissemination of research results, to intervention cost, to differences in cultural preferences, or to a misfit between the intervention format and patients’ needs. Indeed, it is essential that the right intervention be applied to the right patients, at the right time.

To this end, integrating HRQOL and care needs assessments clarify not only the relative severity of symptoms and function, but pinpoint where resources are best directed and for designing the best supportive interventions. It allows health care professionals to provide optimal care by addressing the concerns most important to patients according to their characteristics and aides in improving in health care organization, access to resources, patient-doctor communication, and attention to patients’ psychological distress. What is most important for the individual patient is being treated as a unique person (49). Identifying and addressing specific patients’ needs is a step in this direction.
References


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