Defining Quality of Life

Although most of us have some intuitive sense of what quality of life embodies, a precise definition remains elusive. Quality of life (QoL) is a term that summarizes a range of related, interacting dimensions and the attempts of establishing boundaries around the quality of life construct have proven difficult. For this reason, it is today widely accepted that quality of life assessments should be multi-dimensional in nature (1).

Health-related quality of life is defined as an individual’s perceived physical, mental and social health status affected...
by cancer diagnosis or treatment.

Health-related quality of life measures are defined as well-established questionnaires that measure individuals’ perceptions of their own physical, mental and social health status, or aspects of their health status resulting from cancer and its treatment (2).

QoL may be regarded as person’s subjective impression of his life as a whole. It includes an assessment of general health, satisfaction, fulfillment, ability to cope, happiness, being in control and degree of independence. Assessment of QoL may be regarded as an assessment of cognitive judgements and affective reactions. In medical research, QoL is a multidimensional construct linked with the World Health Organization’s (WHO) definition of health as ‘a state of complete physical, mental and social well-being, and not merely the absence of disease and infirmity’ (3).

Sources of Quality of Life Ratings

It is today universally accepted that the patient is the most appropriate source of information on his or her quality of life. For this reason, many of the quality of life measures are based on direct patient feedback, via interviews or questionnaires. However, there are some situations in which the patients may not be able or willing to provide quality of life ratings, in which cases it should be examined the possibility of employing alternative or proxy informants, like the health care provider or the family.

Role of the Physician in Quality of Life Assessment. Caregivers might be employed as complementary or alternative sources of information on patients’ QoL. The main advantage associated with such observational techniques is that it requires much less time and effort to complete a rating form oneself than it does to arrange for patients to be interviewed or to be assisted in filling out a questionnaire. But this convenience factor may compromise validity and reliability. Several studies have indicated that the reliability of Karnofsky Performance Status (KPS) ratings can be increased by introducing clear definitions of each scale level and by properly training the raters.

Role of the Family in Quality of Life Assessments. Attention has been paid in the recent cancer literature to the potential role of ‘significant others’ and particularly the partners of patients as raters of patients’ quality of life, as they have the opportunity to observe the patient engaging in a wide range of activities over extended periods of time and have better access to the patient’s thoughts and feelings than do health care professionals. The frequency of contact between the patient and proxy rater and the general health condition of the patient may affect concordance level. The quality of the marital relationship play a critical role in the ability of partners to empathize with the patient’s situation and to rate accurately the patient’s QoL. Data from several studies suggest that the higher the level of satisfaction and adjustment within the spousal relationship, and the higher the degree of shared distress, the better will be the concordance between partners’ and patients’ ratings (1). For optimal patient care, it remains important to verify one’s perception by eliciting feedback directly from the patients, whenever possible, but for clinical studies among patient populations at risk of deteriorating self-report capabilities, both patients’ significant others and their healthcare providers can be useful sources of QoL information (4).

Measuring quality of life

Even if there is no consensus in the literature on how the concept of QoL is to be defined it is widely accepted that QoL is multidimensional. No agreement exists as to the number of dimensions and how they are to be measured. The dimensions of the QoL construct are abstract and subjective and therefore indirect methods of measurement like interviews or questionnaires must be used. Assessments of patients’ physical functions by a clinician have often been used as a measure of QoL (Karnofsky’s or ECOG/WH0 performance status). Generic self-report questionnaires including General Health Questionnaire (GHQ), the Sickness Impact Profile (SIP), Nottingham Health Profile (NHP) and McMaster Health Index Questionnaire (MHIQ) have been designed to measure general health applied to QoL, but they are not specifically relevant to cancer patients.

Specific cancer-related instruments have been designed for use in a wide range of diagnostic groups of cancer patients. They should be cancer-specific, brief and easy to understand and respond to and the items should have categorical responses. The patients should be the primary source of data collection. The approach should be multidimensional, and must include subscales assessing physical, functional, psychological and social health. The instrument should have acceptable validity and reliability.

Reliability is a measure of random error. It can be assessed by repeated applications of the same test or indirectly by analysing the internal consistency, which is a measure of the relationships between a set of indicators for the same underlying variable. The last one is often used to determine the reliability of QoL instruments. Validity is defined as the extent to which the result of a method measures the underlying construct in question. It is connected to the degree of systematic measurement error or bias. There are three basic types of validity: criterion, content, and construct validity. Since there is no golden standard for measuring cancer patients’ QoL, indirect approaches need to be used, such as interview-based ratings, and/or analysis of the psychometric properties of the given instrument (how particular instruments relate to each other and their consistency with prior expectations or theory) (3).

Almost 60 different instruments have been used to measure quality of life in cancer patients, including European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC QLQ-C30), Cancer Rehabilitation Evaluation System (CARES), Functional Living Index-Cancer (FLIC).

The EORTC QLQ-C30 was found to be the most widely used cancer-specific instrument. It is a validated cancer-specific questionnaire designed by the European Organization for Research and Treatment of Cancer (EORTC). It is...
multidimensional, cancer-specific, patient-based, designed for self-administration and intended for application across a range of cancer diagnoses.

It takes up to 10 minutes to complete and may be administered by a nurse. This instrument consists of 30 questions designed to measure 15 different QoL key categories: physical functioning (items 1-5), role functioning (items 6-7), cognitive functioning (items 20, 25) emotional functioning (items 21-24), social functioning (items 26-27), general QoL (items 29-30), fatigue (items 10, 12, 18), nausea and vomiting (items 14, 15), pain (items 9, 19) and six single items (8, 11, 13, 16, 17, 28) assess the financial impact of the disease and its treatment, dyspnea, sleep disturbance, appetite, diarrhea and constipation. Items on physical activity comprise 'yes or no' responses whereas the answers to the questions on symptoms range from 'not at all' to 'very much'. The symptoms assessed vary according to the type of cancer being studied (5-8).

It is designed to be supplemented with more disease-specific modules which can assess aspects of QoL of particular importance to various patient subgroups. For example, EORTC QLQ-CR38 and the EORTC QLQ-BLM30 are modules that contain scales examining QoL domains that are relevant to pelvic exenterated patients (9).

The short version of the Cancer Rehabilitation Evaluation System (CARES), CARES-SF (10), is an efficient way to gather information about the day-to-day problems and rehabilitation needs of cancer patients and can be used for research or clinical purposes. The instrument is multidimensional, with well-documented reliability, validity, internal consistency and acceptability to patients, an excellent measure of quality of life. It contains 59 items evaluating five factors: physical (the physical changes and disruption of daily activity caused by the disease or treatment), psychosocial (psychosocial issues, communication and relationship problems), medical, marital (problems associated with a significant marital-type relationship) and sexual (problems related to interest and performance of sexual activity).

Higher scores in functioning scales indicate a higher level of functioning and a better QoL. On the other hand, higher scores in symptoms experience scales correspond to worse or more symptoms and a worse QoL.

Both EORTC QLQ-C30 and CARES are currently validated in several clinical trials in Europe and the USA (3). There are additional issues that may be of interest when studying specific groups of patients. Body image, for example, may be of particular relevance where the treatment involves mutilating surgery, sexual functioning may be an issue for gynecologic, breast, and male genitourinary tract cancers and cognitive functioning may be of particular concern in studies of childhood cancer or adult brain tumors. If we should assume that each domain contributes equally to overall quality of life or if there are significant cross-cultural differences in quality of life domains in terms of their meaning and importance are unanswered concerns.

Our modern day health care systems offer little opportunity for the patients to express their feelings or to talk about their problems. Thus, patients often welcome the opportunity to report their experiences and concerns, even within a formal psychosocial investigation. In a survey of investigators active in the field of psychosocial oncology, the most prevalent problem reported in conducting quality of life studies was obtaining the cooperation of medical staff. Adequate time should be devoted to assuring that the medical staff is familiar with the purpose of psychosocial studies. Frequently, the quality of life component of multicenter clinical trials is optional. The institutions that are willing to undertake such investigations are typically those with academic affiliations or with a strong tradition in clinical research. Of primary importance is the development of patient self-report questionnaires that are comprehensive and psychometrically robust while also being brief enough to be of practical use in clinical settings (1, 2, 5).

Advanced primary or recurrent cancer of the pelvis is a devastating disease characterized by severe pain from bony, muscle or nerve invasion, bladder and bowel problems and renal failure from ureteric obstruction. In the past, most of the patients with extensive pelvic malignancy were offered palliative chemoradiotherapy to control symptoms and to slow disease progression. Pelvic exenteration (PE), an ultraradical procedure, described initially by Brunschwig (11) in 1948 as a palliative approach, is, nowadays, considered a potentially curative treatment in patients with advanced or recurrent pelvic malignancies, including rectal, gynaecological and urological. Exenterative procedures are defined as anterior, posterior, and total and subclassified as suprarectal PE (type 1), infrarectal PE (type 2), and infrarectal PE with vulvectomy (type 3) according to the classification of Magrina et al. (12).

Improvements in surgical technique and perioperative care have contributed to the improved survival following this procedure. The therapeutic role of PE is supported by encouraging survival data from large retrospective series, which demonstrated a 5-year overall survival after PE ranging from 25% to 50% (13). Consequently, a greater proportion of survivors faces recovery challenges and present to healthcare professionals with a range of physical and psychological issues. Besides the impact of cancer diagnosis by itself, the surgical removal of organs accomplishing reproductive functions and the impairment of bowel and urinary functions may have profound psychological implications on women with gynecological malignancies. Therefore, the profiling and understanding of the health-related quality of life is integral to the long-term management of this patients. However, there are few reports in the literature evaluating the QoL in gynecological cancer patients submitted to PE (14-16).

Other than curative role, major surgery can have a palliative character in end-stage gynecologic cancer when severe disease symptoms significantly affect quality of life. Malignant bowel obstruction, unremitting pelvic pain, fistula formation, tumor necrosis, pelvic sepsis, and chronic hemorrhage are among the reasons patients undergo palliative surgeries.
Quality-of-life improvement should be the goal of palliative surgery. Magrina et al. (12) defined palliative exenteration as tumor extension to the lateral pelvic wall or positive pelvic and para-aortic lymph nodes and reported a 5-year survival of 27%. Stanhope et al. (17) used similar criteria with the addition of bony involvement or distant metastases, reporting a median survival of 19 months with 47% of the patients surviving 2 years. However, survival may not be the best measure of success. The reason for these palliative procedures is to alleviate suffering and not necessarily to prolong life.

The great number of domains affected by PE, including physical and sexual function, body image, social roles, psychological well-being and treatment side-effects makes the QoL research a challenge. It is important that the instruments used to measure the postexenterative QoL reflect its multifaceted nature. In order to properly determine the postexenterative QoL scores, it is also important to evaluate the preoperative baseline functioning, as patients have different treatment history, background and expectations (18).

The literature surrounding QoL in patients undergoing PE is limited by heterogeneous data, small sample sizes and short follow-up. In the largest retrospective multicenter study (19) investigating quality of life and emotional distress in gynecological cancer survivors submitted to pelvic exenteration 96 patients were investigated using the EORTC QLQ-C30 questionnaire and its specific subscales: the EORTC QLQ-CX24 (CX24) and EORTC QLQ-OV28 questionnaires. The aim of the study was to identify predictors of poor QoL outcome focusing on the two most representative QoL subscales: Global Health Status (GHS) and body image (BI). A higher number of ostomies (P = 0.012), the creation of a noncontinent bladder (P = 0.009), and of definitive colostomy (P = 0.008) emerged as independent predictors of poorer GHS scores. Older age (P = 0.003), vaginal/vulvar cancer (P = 0.013), total/posterior PE (P = 0.013), higher number of ostomies (P = 0.012), the creation of a noncontinent bladder (P = 0.009) and of definitive colostomy (P = 0.008) emerged as independent predictors of lower BI levels.

Comparing the exenterated group to patients with locally advanced gynecological cancers not receiving radical hysterectomy or PE, it was observed that PE exerts a positive impact on GHS levels, possible because surgical removal raises in patients a stronger feeling of being free from cancer, but a negative impact on BI (20). Similar results were reported by Hawighorst-Knapstein et al. (16) who demonstrated a significantly lower QoL and poorer BI in women with 2 ostomies compared to patients with no ostomy. These findings strongly emphasize the need to make more efforts to achieve an almost complete organ reconstruction, particularly for the gastrointestinal system, to ensure higher QoL levels to long survivors.

This need to perform a more reconstructive surgery should be adequately balanced with potential increased risks of postoperative complications. In fact, the rate of failure of orthotopic or continent neobladder reconstruction after PE in irradiated women is estimated to be approximately of 35% (21). Furthermore, it has to be considered that colorectal preservation after suprapelvic PE in women who previously received radiation therapy has been associated with fistula occurrence rate of 19% and a 30% overall failure rate (22). In this context, considering that PE is currently recommended as the only curative option in previously irradiated patients with localized recurrence, the most promising way for a better incorporation of reconstructive procedures into PE seems to be the introduction in the primary treatment of gynecological cancer of more tailored high-precision radiotherapy approaches such as intensity-modulated radiation therapy (IMRT). Reconstructive surgery at the time of PE could be more feasible after IMRT (23, 24).

The study of Rezk et al. (15), prospectively examines the QoL changes in 16 patients following pelvic exenteration using a large set of psychological instruments: EORTC QLQ-C30, EORTC QLQ-CR38, EORTC QLQ-BLM30, Brief Fatigue Inventory (BFI), Brief Pain Inventory-Short Form (BPI-SF), Instrumental Activities of Daily Living (IADL), the Center for Epidemiologic Studies Depression Scale (CES-D), and the Impact of Events Scale-Revised (IES-R). Overall QoL, ability to perform daily activities, body image and sexual function all declined at 3 months but were near baseline by 12 months after PE. Although, overall, physical function followed a similar trend, it did not return to baseline. At the 12-month interview, patients reported increased gastrointestinal symptoms but significantly less stress-related ideation compared to baseline. Pain levels did not change significantly during the study period. Although mean depression scores also declined postoperatively compared to baseline, overall, these changes did not reach statistical significance. Providers can counsel patients that many, though not all, symptoms in the first 3 months following exenteration are likely to improve as they adapt to their changed health status.

Although, almost two thirds (63%) of the patients expected to experience either large or extreme amount of pain when surveyed prior to the procedure, pain levels did not change significantly during the study period. While the expectation likely represents the patients’ perception of the degree of radicality of this procedure, the actual experience probably reflects the efficacy of modern pain control modalities following radical pelvic surgery. In this patient cohort, pain control was not a significant issue. The longitudinal changes in the social and cognitive function mean scores did not reach statistical significance nor did those of the financial impact domain and other symptoms.

In contrast to these findings, in the report of Hawighorst-Knapstein et al. (16) comparing QoL of patients who underwent Wertheim’s procedure to that of those who underwent PE for cervical cancer, body image mean scores continued to worsen over time, probably due to a more frequent use of postoperative adjuvant treatment. In addition, two-ostomy patients’ global QoL and body image scores worsened over time. Although stratifying PE patients according to the number of ostomies may reveal real differences in QoL, for a better definition of QoL, PE patients may be best stratified according to the type of
diversion performed, as the impact of a urostomy on QoL may be different from that of a colostomy.

In the study of J. Khalil et al. (25), assessing the QoL in 110 patients for three multi-item scales (symptom experience, body image, and sexual/vaginal functioning) and six single-item scales (lymphedema, peripheral neuropathy, menopausal symptoms, sexual worry, sexual activity, and sexual enjoyment) more lymphedema, less sexual functioning and enjoyment and less satisfaction with their body image was found in cervical cancer group, but on the multivariate analysis only social support and spiritual well being were defined as predictors of QoL.

An objective assessment (26) of postoperative psychologic, social, and sexual functioning indicated significant differences between the sexually active and nonactive patients and between the patients with a neovagina and those with no vaginal capacity only in the area of sexual functioning, not in psychologic or social (eg, visiting friends, relatives, neighbors) and free-time (eg, hobbies, community activities, reading) activities. The satisfactory levels of social and free-time activities may be due partially to the fact that the majority of the exenteration patients are unemployed. As such, the patients in this sample may have had more freedom in their schedules to maintain social/free-time activities than did the normative samples. This may indicate that if women are able to maintain their activities, they may be less prone to psychologic distress, depressive symptoms (eg, crying, sleep problems, weight loss, thoughts of self-injury) and attitudes (eg, feelings of failure or worthlessness, discouragement about the future, loss of interest in other people).

All women believed there should be discussion regarding sexuality with them and their partners before and following surgery by a trained individual, comfortable in such matters.

A profile of psychosocial adjustment for the pelvic exenteration patients in this sample has emerged. Psychologically, these women remain mildly distressed and depressed. They engage in reasonable levels of social and free-time activities. Disruption of sexuality, however, is an obvious outcome for virtually all patients. This includes reduction in the frequency of sexual activity, low sexual arousal and satisfaction, and disruption of sexual confidence and body image. These difficulties are more or less distressing to a patient depending on the availability of a sexual partner and the patient’s own desire for the continuation of her sexual life.

Limited information exists in the literature regarding QoL before and after pelvic exenteration surgery for rectal cancer. Previous research investigating these patients suggested that longer-term survivors of pelvic exenteration have a reasonable QoL compared with patients undergoing a routine resection of a rectal primary cancer.

Jessica Beaton et al. (27) conducted a study to determine if preoperative body mass index (BMI) is associated with 30-day morbidity, length of hospital stay and/or quality of life (QoL) in patients undergoing pelvic exenteration surgery for recurrent and locally-advanced rectal cancer. QoL was measured using the Functional Assessment of Cancer Therapy - Colorectal (FACT-C) questionnaire. A lower BMI preoperatively was associated with a longer length of hospital stay and a trend towards a greater number of postoperative complications, but the nutritional status was not associated with long-term QoL in this patient group.

The study of Quyn et al. (28) supports an aggressive approach to advanced primary rectal cancer and lends weight to the oncological role of pelvic exenteration describing the quality of life outcomes over 12 months for 104 patients having pelvic exenteration for locally advanced primary rectal cancer at a specialised centre for pelvic exenteration. The average FACT-C score returned to pre-surgery QoL by 2 months after surgery, and the average QoL continued to improve over the first year. The same results were obtained in a prospective cohort study (18) on 117 patients with recurrent rectal cancer in which the non-exenteration patients' QoL gradually declined over 12 months while exenterated patients' QoL declined, then recovered. Baseline QoL score, gender and bony resection were significant predictors of QoL score at 12 months.

Comparing long-term QoL for patients with primary rectal cancer undergoing abdominal perineal resection versus PE, the QoL recovery seems to be similar, thus patients should not be denied exenterative surgery based on perceived poor QoL (29). In a retrospective study, comparing the modified ileoceleal pouch with the ileal conduit in anterior or total pelvic exenteration Forner et al. (30) found that the mode of urinary diversion has little influence on the quality of life in patients with advanced genital cancer.

Reconstructive surgical procedures are often necessary to enhance wound healing, decrease acute and chronic morbidity and to restore the anatomic form and function. Many reconstruction techniques are available including skin grafting, simple tissue transposition flaps, fasciocutaneous flaps and myocutaneous flaps. Free microsurgical flaps may be utilised so that no compromise in terms of the extent of the oncological resection has to be accepted. Pelvic/vaginal reconstruction plays a major role in facilitating wound healing, minimizing significant morbidity and improving patient quality of life and functional outcomes (30,31).

The importance of quality of life assessment

Quality of life assessments has been successfully used for a range of research purposes in oncology, including: describing the nature and extent of functional and psychosocial problems confronting patients at various stages of the disease; establishing norms for psychosocial complications among specific patient groups; screening of patients for possible behavioral or psychopharmacologic interventions; monitoring the quality of care, improving the way in which treatment is delivered; evaluating the efficacy of competing medical or psychosocial interventions. For these reasons, systematic QoL assessment should become an integral part of cancer management (1).

P. Ganz et al. (32) observed a statistically significant relationship between patient-rated QL (high and low) and survival time. Many studies reported that the global or the overall quality of life was a significant independent
predictor of survival. A recent meta-analysis of the relationship between baseline quality of life data from the EORTC clinical trials and survival indicated that physical functioning was a significant independent prognostic factor (33). As suggested by Gotay et al. (34) there are several explanations for the association between health-related quality of life data and survival duration in cancer outcome studies. The authors summarized four possible explanations: quality of life measures include different items and thus provide more sensitive information than traditional performance status and toxicity measures; quality of life data especially those collected at baseline before disease progression could pick up relevant information earlier than established clinical prognostic factors; quality of life data are markers of patients' behaviour because they relate to diagnosis, treatment and subsequent outcomes of the disease; and quality of life data are markers of individual characteristics such as personality style and adapting coping strategies, which affect the disease process and outcomes in cancer patients.

Several authors have reported on the utility of incorporating information obtained through evaluating QoL into identifying rehabilitation needs, designing effective educational interventions and characterizing those patients who are most suitable for these interventions. Evaluating the impact of exenterative surgery on QoL may help providers to better assess mental health and supportive services and possibly avoid long-term sequelae (15).

Despite their demonstrated utility, inclusion of quality of life parameters in clinical trials remains the exception rather than the rule. The low rate of incorporating psychosocial parameters into clinical trials derives, in part, from the unresolved issues relating to measurement, research design, and study implementation that impede the routine introduction of quality of life end points in the rigorous confines of the clinical trial.

**Conclusions**

Quality of life evaluation must be an end point in clinical trials. Although patients report some decline in physical function after pelvic exenteration, most adjust well, returning to almost baseline functioning within a year. The reduction of ostomies seems to be the most effective factor to improve patients' QoL. Several unmet needs emerge in pelvic malignancies survivors, for this reason a long-term psycho-oncological support is recommended.

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