Consideration of Quality of Life in Cancer Survivorship Research

Paul B. Jacobsen and Heather S.L. Jim

Abstract

Quality of life assessment has a number of important applications in research on cancer survivors. These applications include use in observational studies to characterize the nature and extent of problems patients experience as well as use in randomized controlled trials to evaluate the relative impact of different cancer treatments or to evaluate the efficacy of interventions designed to improve patient well-being. The aims of this article are to provide an overview of the construct of quality of life and describe strategies commonly used to measure quality of life in adult cancer survivors. In addition, several priorities for future research are identified that involve how quality of life is measured, in whom it is measured, and what uses are made of quality of life data in the clinical care of cancer survivors. Cancer Epidemiol Biomarkers Prev; 20(10); 2035–41. ©2011 AACR.

Introduction

Research on the quality of life of cancer survivors has increased steadily in recent years. Using Medline as a metric, a search of articles published in 1995 indexed under the combination of “quality of life,” “neoplasms,” and “survivors” yielded 27 publications; in 2010, this number had increased to 293 publications. The growing number of publications is consistent with increasing recognition that endpoints in addition to survival and disease-free survival are important when considering the impact of cancer treatments. In contrast to studies evaluating how long patients are surviving, research on quality of life addresses the key question of how well patients are surviving. As described in the following text, quality of life outcomes encompass patients’ self-reports of their well-being and functioning across a number of health-related domains.

Quality of life assessment has found a number of important uses in research on cancer survivors. One of the most common applications has been in observational studies. In this context, quality of life data can be used to identify the nature and extent of problems patients experience in relation to such variables as type of disease, the types of treatments received, and the time that has elapsed since treatment completion. This information has considerable relevance for efforts to inform patients of the expected consequences of specific treatments and for efforts to identify the expected rehabilitative needs of cancer survivors. Another application has been as an outcome in randomized controlled trials. Inclusion of a quality of life endpoint in cancer treatment studies, such as phase III clinical trials, can be particularly useful when the treatments being compared yield equivalent results for efficacy against disease endpoints. Under these circumstances, the preferred treatment may be identified on the basis of differences in quality of life. Quality of life has also been used as the sole endpoint in studies designed specifically to improve the physical or mental well-being of people with cancer. In these studies, quality of life data can yield important information about whether the intervention being evaluated should be disseminated or implemented as part of routine clinical care. A fourth and growing application has been the use of quality of life assessments as part of health services research. For example, quality of life data can be used as a means of evaluating the quality of care received by cancer survivors who experience persistent or late effects of treatment.

With this information as background, the aims of this article are to (a) provide an overview of the construct of quality of life; (b) describe strategies commonly used to measure quality of life in adult cancer survivors; and (c) identify priorities for future research on quality of life in cancer survivors.

Quality of Life Overview

The World Health Organization (1) defines quality of life as “individuals’ perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad-ranging concept, incorporating in a complex way individuals’ physical health, psychological state, level of independence, social relationships, personal beliefs, and their relationships to salient features of their environment.” Quality of life is a multidimensional construct most often assessed via self-report. It is individual-centered because the
individual must evaluate his or her own functioning across a number of domains. The domains differ somewhat across measures, but there is general consensus that quality of life encompasses physical functioning, emotional functioning, social functioning, role functioning, and overall quality of life (2). Physical functioning refers to the impact of physical health on daily activities such as self-care and ambulation. Emotional functioning describes depression and anxiety. In cancer-related measures, emotional functioning also refers to fears about illness and recurrence. Social functioning refers to the ability to engage in meaningful social interactions, activities, and relationships. Role functioning indicates the degree to which individuals are able to carry out their usual roles at home, school, work, and in the community. Finally, overall quality of life refers to individuals’ global assessment of functioning in all domains of life. As described in the following text, many quality of life measures used with cancer patients assess additional domains that reflect issues germane to certain forms of cancer, forms of treatment, or points on the disease/treatment continuum.

Measurement of Quality of Life

Although researchers and clinicians agree that quality of life is an important outcome, there is currently no consensus about which measure should be used. Examples of commonly used measures in oncology settings are shown in Table 1. These measures can be grouped into 4 major categories: (a) general measures, (b) cancer-specific measures, (c) disease- or treatment-specific measures, and (d) measures specific to a point on the cancer continuum (e.g., survivorship, end of life). These 4 categories encompass a wide variety of questionnaire lengths and formats, including traditional Likert scale and yes/no responses, interviews, visual analog scales, patient and proxy measures, and computerized adaptive testing. Many of these measures have been translated into multiple languages.

General measures of quality of life are appropriate for both medically ill and healthy populations. Several of these measures, such as the Medical Outcomes Study Short Form—36 (SF-36; refs. 3, 4) and World Health Organization Quality of Life Assessment Instrument (WHOQOL-100; ref. 5), are widely used, well validated, and have population-based normative data. In addition, the WHOQOL-100 was developed to be a valid measure of quality of life across cultural settings (5). Both measures have been translated into several languages. Both also have shorter versions to reduce participant burden (i.e., SF-12, SF-8, WHOQOL-BREF; refs. 6–8). General quality of life measures such as these are advantageous because they enable comparisons between cancer patients, patients with other illnesses, and healthy individuals. They are limited, however, in that they typically do not assess symptoms commonly resulting from cancer and cancer treatment, such as nausea/vomiting, hair loss, and pain. They also may not assess domains of quality of life that are often affected by cancer or its treatment, such as cognitive and sexual functioning.

Cancer-specific measures of quality of life provide a more comprehensive assessment of symptoms and domains likely to be important to cancer patients. They typically cannot be used to compare quality of life in cancer patients to that in other groups; an exception is the Functional Assessment of Cancer Therapy—General (FACT-G) questionnaire (9). The FACT-G assesses physical, functional, social, and emotional domains of quality of life, as well as global quality of life. Published normative data are available for the FACT-G using 21 of the 27 total items applicable to noncancer samples (10). Other cancer-specific measures do not have population normative data but encompass slightly different domains of quality of life. For example, the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30; ref. 11) assesses physical, social, cognitive, emotional, and role functioning. It also includes 3 symptom scales—fatigue, pain, and nausea/vomiting. The Cancer Rehabilitation Evaluation System—Short Form (CARES-SF; ref. 12) assesses physical, psychosocial, and sexual functioning as well as marital interaction and interaction with medical staff. Investigators may wish to tailor assessment of quality of life to their research question by selecting a cancer-specific measure that most closely reflects their constructs of interest. For studies comparing quality of life across cancer and noncancer samples, investigators may wish to include both general and cancer-specific measures of quality of life to facilitate group comparisons, while still providing detailed quality of life information in the cancer sample.

Assessment of quality of life in cancer patients can be further tailored through the use of measures specific to a particular disease, treatment, or point on the cancer continuum. Numerous measures of this type are available through the FACT or EORTC measuring systems. For example, the FACT includes questionnaires specific to symptoms of breast, colorectal, ovarian, and lung cancers, among others, as well as questionnaires for patients treated with EGFR inhibitors, taxane, biologic response modifiers, and blood and marrow transplant (13). FACT questionnaires are also available for specific symptoms such as fatigue and neurotoxicity (13). These questionnaires, such as the FACT-B (breast cancer) and the FACT-P (prostate cancer), are derivations of the FACT-G and include an added subscale that assesses targeted concerns related to a specific cancer type. Similarly, the EORTC has modules for lung, breast, head and neck, prostate, ovarian, and other types of cancer as well as modules for high dose chemotherapy, neurotoxicity, bone metastases, fatigue, elderly patients, palliative care, and others (14). Additional measures specific to disease, treatment, and point on the cancer continuum have been developed independently of the FACT and EORTC.
Table 1. Examples of commonly used measures of quality of life in cancer patients

<table>
<thead>
<tr>
<th>Measure name</th>
<th>Abbreviation</th>
<th>Domains assessed</th>
<th>Format</th>
<th>Number of items</th>
<th>Validation sample(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General measures</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>EuroQol (24)</td>
<td>EuroQol-5D</td>
<td>Subscales: mobility, self-care, usual activity, pain, anxiety/depression; overall health state</td>
<td>Self-report, observer, proxy interview</td>
<td>5 items in Likert scale format plus a visual analog scale</td>
<td>General European populations, medical patients</td>
</tr>
<tr>
<td>Medical Outcomes Study Short Form—36 (43)</td>
<td>SF-36</td>
<td>Subscales: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, mental health; composite scores: physical, mental</td>
<td>Self-report</td>
<td>36 items in yes/no or Likert scale format</td>
<td>General US populations, medical patients</td>
</tr>
<tr>
<td>Medical Outcomes Study Short Form—12 (8)</td>
<td>SF-12</td>
<td>Subscales: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, mental health; composite scores: physical, mental</td>
<td>Self-report</td>
<td>12 items in yes/no or Likert scale format</td>
<td>General US populations, medical patients</td>
</tr>
<tr>
<td>Quality of Life Index (21)</td>
<td>QLI</td>
<td>Total score</td>
<td>Physician report</td>
<td>5 items in Likert scale format</td>
<td>Cancer patients</td>
</tr>
<tr>
<td>World Health Organization Quality of Life Assessment Instrument (1)</td>
<td>WHOQOL-100</td>
<td>Subscales: physical, psychological, level of independence, social relationships, environment, spirituality/religion/personal beliefs; overall QOL</td>
<td>Self-report</td>
<td>100 items in Likert scale format</td>
<td>World population, medical patients, cancer patients</td>
</tr>
<tr>
<td>World Health Organization Quality of Life Assessment Instrument—Brief (5)</td>
<td>WHOQOL-BREF</td>
<td>Subscales: physical, psychological, social relationships, environment; overall QOL</td>
<td>Self-report</td>
<td>26 items in Likert scale format</td>
<td>World population, medical patients</td>
</tr>
<tr>
<td>Patient-Reported Outcomes Measurement Information System² (33, 34)</td>
<td>PROMIS</td>
<td>Examples of item banks: global health scale, physical function, emotional distress, social health</td>
<td>Self-report</td>
<td>Item bank, short form, computer adaptive testing available</td>
<td>General US population, patients with chronic medical conditions</td>
</tr>
<tr>
<td>Cancer-specific measures</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer Rehabilitation Evaluation System—Short Form (44)</td>
<td>CARES-SF, CIP</td>
<td>Subscales: physical, psychosocial, sexual, marital, medical interaction; global QOL</td>
<td>Self-report</td>
<td>139 items in Likert scale format</td>
<td>Patients with heterogeneous cancer diagnoses</td>
</tr>
<tr>
<td>European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (11)</td>
<td>EORTC QLQ-C30</td>
<td>Functioning scales: physical, social, role, cognitive, emotional; symptom scales: fatigue, pain, nausea/vomiting; global health/QOL scale</td>
<td>Self-report</td>
<td>30 items in yes/no or Likert scale format</td>
<td>Patients with heterogeneous cancer diagnoses</td>
</tr>
<tr>
<td>Functional Assessment of Cancer Therapy—General (9)</td>
<td>FACT-G</td>
<td>Subscales: physical, functional, social, emotional, relationship with doctor; total score</td>
<td>Self-report</td>
<td>28 items in Likert scale format</td>
<td>Patients with heterogeneous cancer diagnoses</td>
</tr>
</tbody>
</table>

(Continued on the following page)
<table>
<thead>
<tr>
<th>Measure name</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Functional Living Index—Cancer (22)</td>
<td>FLIC</td>
<td>Subscales: physical, psychological, social, current well-being, gastrointestinal symptoms; total score</td>
<td>Self-report</td>
<td>22 items in visual analog scale format</td>
<td>Patients with heterogeneous cancer diagnoses</td>
</tr>
<tr>
<td>Measures for cancer subpopulations</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>FACT modulesb (9)</td>
<td>Various</td>
<td>Examples of modules: breast cancer, blood and marrow transplant, lung cancer, prostate cancer</td>
<td>Self-report FACT-G plus subpopulation-specific items in Likert-scale format</td>
<td></td>
<td>Various subpopulations</td>
</tr>
<tr>
<td>EORTC modulesc (11)</td>
<td>Various</td>
<td>Examples of modules: ovarian cancer, gastric cancer, brain cancer</td>
<td>Self-report EORTC QLQ-C30 plus subpopulation-specific items in Likert scale format</td>
<td></td>
<td>Various subpopulations</td>
</tr>
<tr>
<td>Expanded Prostate Cancer Index Composite (45)</td>
<td>EPIC</td>
<td>Subscales: urinary incontinence, urinary irritative/obstructive, sexual, bowel, hormonal symptoms</td>
<td>Self-report</td>
<td>26-item short form in Likert-scale format; other versions include SF-12</td>
<td>Prostate cancer patients</td>
</tr>
<tr>
<td>Lung Cancer Symptom Scale (46)</td>
<td>LCSS</td>
<td>Self-report subscales: symptoms, total symptomatic distress, activity status, overall QOL; observer subscale: symptoms</td>
<td>Self-report, observer</td>
<td>9 items in visual analog scale; observer: 6 items in Likert scale format</td>
<td>Lung cancer patients</td>
</tr>
<tr>
<td>Therapy Impact Questionnaire (47)</td>
<td>TIQ</td>
<td>Subscales: physical symptoms, functional status, concomitant emotional and cognitive factors, social interaction</td>
<td>Self-report</td>
<td>36 items in Likert scale format</td>
<td>Advanced cancer patients</td>
</tr>
<tr>
<td>Quality of Life in Adult Cancer Survivors (15)</td>
<td>QLACS</td>
<td>Generic subscales: physical pain, negative feelings, positive feelings, cognitive problems, sexual problems, social avoidance, fatigue; Cancer-specific subscales: financial problems, distress about family, distress about recurrence, appearance concerns, benefits of cancer; generic summary score; cancer-specific summary score</td>
<td>Self-report</td>
<td>47 items in Likert scale format</td>
<td>Breast cancer survivors</td>
</tr>
<tr>
<td>Quality of Life at the End of Life (48)</td>
<td>QUAL-EC</td>
<td>Subscales: symptom severity, quality of relationship with healthcare provider, preparation for end of life, feeling of life completion</td>
<td>Self-report</td>
<td>54 items in Likert scale format</td>
<td>Medical patients at end of life, cancer patients at end of life</td>
</tr>
</tbody>
</table>

*A current listing of PROMIS item banks is available at http://www.nihpromis.org.

*bA full listing of FACT modules is available at http://www.facit.org.

cA full listing of EORTC QLQ-C30 modules is available at http://groups.eortc.be/qol.
An important example relevant to the topic of this report is the Quality of Life in Adult Cancer Survivors (QLACS) measure (15, 16). Development of this measure was driven, in part, by the view that existing cancer-specific measures were designed primarily to capture the acute effects of diagnosis and treatment. Accordingly, they may not adequately assess problems that can persist long after treatment completion such as pain, fatigue, cognitive difficulties, sexual difficulties, and body image concerns (17). In addition, these measures may not capture issues more likely to emerge after treatment completion such as financial issues and recurrence concerns or perceptions of the positive impact of the cancer experience on relationships and life satisfaction (17). Consistent with a focus on long-term (i.e., >5 years) cancer survivors, the QLACS assesses 7 generic domains of quality of life (i.e., physical pain, negative feelings, positive feelings, cognitive problems, sexual problems, social avoidance, and fatigue) and 5 cancer-specific domains (i.e., financial problems resulting from cancer, distress about recurrence, appearance concerns, and benefits of cancer).

Most quality of life measures are intended to be patient self-administered questionnaires. However, some specifically allow interview administration when necessary (e.g., SF-36, FACT-G). Interview administration is useful for patients who are unable to read, are visually impaired, or have difficulty writing (e.g., due to neuropathy or tremors). Some research suggests that patients may be less likely to report poor quality of life when responding to an interview as compared with completing questionnaires (18, 19), although evidence is conflicting (20). Very short measures using visual analog scales are an alternative to interviews for patients who have low literacy levels or are otherwise unable to fill out longer questionnaires. Quality of life measures using visual analog scales include the Uniscale (21), Functional Living Index—Cancer scale (22), and the Holmes QOL Checklist (23). In addition, the EuroQol-5D includes a single item assessment of global quality of life by using a visual analog scale (24, 25). Proxy reports of quality of life offer an alternative to assessing quality of life when patients are unable to communicate (e.g., end of life). Proxy measures can also be used to corroborate patients’ self-reports of quality of life or explore perceived differences in quality of life between patients, caregivers, and clinical staff. For example, the Quality of Life Index (21) was designed to be completed by physicians, whereas the EuroQol-5D offers a proxy version for caregivers (24, 25). Previous research suggests that physicians tend to overestimate patients’ quality of life compared with patients’ own reports (26), whereas caregivers tend to underestimate patients’ quality of life (27). Agreement between caregivers’ and patients’ ratings of quality of life tends to be highest when patients are experiencing very good or very poor quality of life; concordance tends to be worse for patients with intermediate quality of life (28, 29). Proxy reports tend to be most accurate for objective domains of quality of life (e.g., physical functioning) and least accurate for subjective domains of functioning (e.g., emotional well-being, global quality of life; ref. 27). As such, patients should be the primary source of information about their quality of life, whenever possible.

Priorities for Future Research

The marked increase in publications on quality of life in cancer survivors in recent years suggests widespread recognition of the value of conducting research on this topic. For the field to continue to progress, however, important issues still need to be addressed related to how quality of life is measured, in whom it is measured, and what uses are made of quality of life data.

The numerous self-report measures of quality of life available for use with cancer survivors can be viewed as both a strength and a weakness. On the positive side, researchers have the ability to choose the depth and breadth of information they wish to obtain. On the negative side, the frequent use of different measures in different studies seriously limits the ability to directly compare findings across publications. A preferable situation scientifically would be one in which researchers routinely administered the same core measure(s), thus facilitating comparability, with additional study-specific measures used as appropriate. Greater consistency in quality of life measurement across studies may be facilitated by the ongoing Patient-Reported Outcomes Measurement Information System (PROMIS) initiative. This cooperative group program of research is designed to develop, validate, and standardize item banks for measurement of patient-reported outcomes across many common medical conditions, including cancer (30, 31). Using contemporary test construction methodology that builds on existing instruments, the initiative has produced item banks and scales for many commonly measured quality of life domains (32). Investigators can choose to administer an entire item bank for a given domain of quality of life, a shorter form, or a computer adaptive test. The computer adaptive test dynamically selects items to administer from an item bank based on the patient’s responses to previous items. As a result, quality of life is assessed with the smallest possible number of items, thus reducing patient burden. Measures of several domains of quality of life (e.g., global health, physical function, emotional distress) have been created and more are currently under development (33, 34). Inclusion of PROMIS items and scales in survivorship studies thus represents one way to improve the comparability of findings across studies.

A large number of studies of quality of life in cancer survivors are based on convenience sampling conducted at a single recruitment site. Although useful in promoting greater understanding of the quality of life issues facing cancer survivors, many of these studies suffer from important limitations about the ability to...
conduct adequately powered subgroup analyses and the generalizability of their findings. Thus, in addition to smaller scale studies, there is a need for research based on larger cohorts of survivors that are recruited from multiple sites and/or by using population-based recruitment strategies. Examples of survivorship studies incorporating quality of life assessments that have used this recruitment approach include the Childhood Cancer Survivor Study (35) and the American Cancer Society’s Studies of Cancer Survivors (36). A complementary strategy to assembling large cohorts of cancer survivors is to embed quality of life measures in large ongoing population-based surveys that include cancer survivors. This strategy has the added advantage of also generating data on people without cancer that can be used for comparison purposes. An example of this approach is the National Health Interview Survey (NHIS; ref. 37), which includes periodic supplements devoted to cancer control. In the past, the NHIS has been used to carry out comparisons of cancer survivors with individuals having no history of cancer in terms of their health and disability status (38), health behaviors (39), and mental health service use (40). Together with the data collected from larger survivor cohorts, the NHIS and similar national surveys could provide a means to monitor for changes in quality of life over time as new forms of cancer treatment (e.g., targeted therapies) are introduced into routine clinical practice.

Among the essential components of survivorship care identified in a seminal Institute of Medicine Report (17) was the delivery of interventions for the consequence of cancer and its treatment. The consequences identified include issues assessed by many quality of life instruments, such as pain, fatigue, psychological distress, and problems in role functioning (17). Accordingly, quality of life measures could play an important role in the routine clinical care of cancer survivors. For example, patients’ responses to these measures could be used to inform the content of survivorship care plans that are recommended as an important means of improving the quality of care of cancer survivors (17). The use of quality of life measures in this manner is supported by research showing that providing clinicians with patients’ responses to these measures during the active treatment period improves symptom management and overall quality of life (41, 42). Similar research needs to be conducted in the posttreatment period to determine whether development and implementation of survivorship care plans has a positive impact on the quality of life of cancer survivors. Supportive evidence would show that assessing quality of life has utility as both a process and an outcome of survivorship care.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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