Quality of Life Assessment in Cancer Clinical Trials—It’s Time To Catch Up

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Quality of life is a concept that is not unique to medicine (1). A news report in Science a few years ago addressed the lack of quality of life likely in the nuclear winter aftermath of World War III (2). The phrase is familiar to all of us and has crept into ward rounds and journal advertisements, as if we all knew and agreed on what it means. But when we try to define it, we discover that the precise meaning is neither clear nor easily agreed on. This is, of course, because quality of life has such an important subjective component. Each of us can give only a personal interpretation.

Calman (3) provided one helpful definition when he wrote that quality of life is “the extent to which a person’s hopes and ambitions are matched and fulfilled by experience.” This interpretation carries the important implications that the same experiences may have different quality of life meaning for different individuals and that changing expectations over time can result in altered perceptions of quality of life in similar circumstances. Notwithstanding the elusive nature of the quality of life concept, there are several elements that patients, families, and health care professionals commonly accept as important to the patient’s quality of life experience (4):

(a) functional capacity (ability and energy) for daily routine, social interactions, intellectual activity, emotional reactions and adjustments, and economic independence;
(b) self-perceptions of wellness or its absence; and
(c) symptoms of disease or treatment.

Quality of life evaluations in patients with cancer have not been a routine component of cancer clinical trials in the United States, despite the mission statement of the Division of Cancer Treatment of the National Cancer Institute: “Research aimed at improving survival and quality of life for persons with cancer is of highest priority to CTEP [the Cancer Therapy Evaluation Program]” (5). The failure to systematically evaluate quality of life end points in cancer clinical trials can be attributed to several factors. Oncology physicians who have been responsible for setting policy and for designing and carrying out clinical trials have always hoped that the magic bullet would be just around the corner. We would cure large numbers of patients if we could come up with the right combination or new agent, as happened in acute lymphocytic leukemia of childhood. Energies and dollars have been understandably concentrated in a manner calculated to achieve that goal as rapidly as possible. In addition, most physicians have not been comfortable working with social scientists, whose end points were mistakenly viewed as “soft” and whose tools were cumbersome to use. Thus, psychosocial and quality of life evaluations, with a few notable exceptions, have not become part of most major clinical trials of cancer therapy.

There are encouraging signs that more regular inclusion of quality of life end points as integral parts of major clinical trials will come about in the next few years (6,7). In this issue of the journal, Moinpour and associates review the development of policies to guide the introduction of quality of life end points in the Southwest Oncology Group cancer clinical trials. Their work is a welcome venture in the right direction, and it should prove useful to other cancer clinical trials groups. Their recommendations for strategies to incorporate quality of life assessment in clinical trials research are based (a) on a sound understanding of the potential importance of quality of life evaluations in cancer clinical trials and (b) on the unique practical problems encountered in performing social science research in a busy oncology clinic.

While the specific policy recommendations for the Southwest Oncology Group represent one good approach that will guide the introduction of quality of life assessment into clinical trials, other strategies may be equally well chosen and effective for other groups. For example, Moinpour and colleagues have recommended phase III trials as the place to begin assessment of quality of life. Some phase II studies would be equally appropriate. Gathering quality of life information about a phase II combined-modality program for head and neck cancer that was expected to result in major toxic effects and dysfunction could provide critical data about the effect of therapy on the severity and duration of pain, appetite, ability to eat, sleep patterns, psychological state, and social interactions. This information would greatly increase our understanding of the regimen being used. Such data might also be helpful to investigators in changing the design of a subsequent phase III trial or building in checkpoints for early intervention to minimize symptoms and dysfunction during the phase III study. The knowledge gained from these evaluations could result in (a) an increase in the number of patients who complete and benefit from the prescribed regimen and (b) a more easily completed study.

The recommendation of Moinpour and co-workers that patient-based measures should supplement physician judg-
ments of treatment-related toxic effects is critical. Jachuck and colleagues (8) showed that although 100% of physicians thought their patients had improved quality of life after starting antihypertensive therapy, only 48% of the patients felt improvement, 44% felt no change, and 8% felt worse. In contrast, assessments by relatives indicated that the quality of life for more than 90% of the patients was worse.

The choice of instruments to be used in measurement of factors affecting quality of life has been one of the greatest impediments to the introduction of this kind of end point into clinical trials. As noted by Moinpour and associates, Aaronson and the European Organization for Research and Treatment of Cancer (9) have been working on the problem for years. The development of a modular approach to quality of life evaluations offers a practical solution to the difficulty previously posed by lengthy standardized instruments. These measures were cumbersome for patients and clinic personnel and did not provide those evaluating the clinical trial with clinically relevant information about the changes in quality of life resulting from the treatment. How effective the modular instruments will be has yet to be demonstrated in major clinical trials.

The Southwest Oncology Group approach of using standard instruments with established psychometric properties has the advantage that validity and reliability are known, though not necessarily for patients undergoing cancer therapy. However, this approach has the disadvantage that items not of interest in the clinical trial setting will be measured and disease-specific impairments and protocol-specific toxic effects may be missed.

The Eastern Cooperative Oncology Group plans to use two parallel methods. In some of our trials, we will rely primarily on established instruments with known psychometric properties. Also under development is a Function, Symptom, and Perception of Wellness Evaluation (FSPE) instrument containing core questions that will be relevant regardless of the type of cancer or treatment and modular questions that will be specific for the type of cancer, treatment, or protocol. Establishment of psychometric properties and refinement of the instrument will be ongoing processes. During the period of introduction of quality of life assessment into clinical trials, there will be room for several approaches as we learn to garner this new type of information in cancer clinical trials.

If the introduction of quality of life evaluations into the mainstream of cancer clinical trials is to be successful, support will be needed from several fronts. The National Cancer Institute’s continued commitment (5,10) and willingness to provide financial support through both the Cancer Therapy Evaluation Program of the Division of Cancer Treatment and the Centers and Community Oncology Program of the Division of Cancer Prevention and Control will be essential if the cooperative groups and their member institutions are to make progress in this area. The cooperative groups themselves must be willing to share responsibility for protocol design with social scientists, to allocate statistical and data-management support, and to convince physicians and nurses at member institutions of the importance of quality of life endpoints in cancer therapy evaluation. Social scientists must learn how to work with the limitations of the cooperative group setting while capitalizing on its extraordinary resources for quality of life research. Communication among researchers from different cooperative groups should be fostered, and intergroup studies should be undertaken when it is scientifically and practically appropriate.

There is a lot of catching up to do before quality of life assessments will achieve their rightful place as reliable and valid end points in cancer clinical trials. We are optimistic that the process of introducing such evaluations into the cooperative group trials will be speedy and smooth, for they are greatly needed to help physicians and patients to better understand the benefits and burdens of cancer therapy.

References