Quality of Life Measurements: A Soft Outcome—Or Is It?

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Abstract

In oncology research, quality of life (QOL) has been identified as the second most important outcome, with survival being the most important. The integration of QOL assessments into clinical practice and research presents some unique challenges. QOL outcomes are sometimes perceived to be soft, as opposed to the type of outcomes that provide hard end points or factual data and can be easily defined quantitatively. The softness of QOL outcomes relative to survival and tumor response is cited as a particular barrier to implementation and interpretation of results. This article reviews the importance of QOL to clinical practice, discusses the perceived softness of QOL, and compares the roles of symptoms and QOL scores as they relate to disease progression and tumor response. Providing sound QOL data to healthcare professionals and patients is essential to enable truly informed decision-making.

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How important is quality of life (QOL) as an outcome? Assertions have been made in oncology that QOL is second in importance only to survival.[1] The medical literature has long-standing evidence for the support of QOL as an integral part of medical care[2] and that securing the happiness of the patient is worthwhile in addition to prolonging life.[3] Despite this long-standing philosophical assertion, the application of QOL as a research outcome lags behind the long-standing assertion of its importance. This article addresses the importance of QOL data in patient care; provides a discussion of why QOL has often been considered a softer outcome than measures such as tumor response; and discusses the relative roles of symptoms and QOL scores in studies of disease progression and tumor response.

Importance of QOL in Patient Care

Medical science demands data to support the efficacy of various treatments and the importance of particular outcomes. Evidence has accumulated in recent years in support of QOL measures being important to treatment outcome. A patient's QOL has been seen to be prognostic for survival in a number of settings.[4-6] Patient fatigue has been identified as both a prognostic and mitigating factor in the efficacy of cancer treatments.[7,8]

QOL data can be particularly helpful when 2 treatments reveal similar survival outcomes but exhibit differences in QOL outcomes. For example, research has demonstrated that breast conservation followed by radiation therapy for breast cancer has a survival outcome equivalent to that of modified radical mastectomy. These data held the expectation that women would experience fewer physical symptoms, less psychological distress, and less sexual dysfunction while having improved body image and improved marital satisfaction. However, when research data were collected, patients indicated that the only advantage was in improved body image.[9-12] For some patients, the simple matter of having a choice is the vari-

able that impacts QOL rather than the actual procedure that is selected. One year after the procedure, women who had a choice between breast conservation and mastectomy reported less depression than women who did not have a choice.[13]

Although data have only recently demonstrated its efficacy, prophylactic mastectomy had been performed for a number of years because of its assumed efficacy.[14] Clinicians have long verbalized strong opinions about the outcomes from this surgery despite the lack of systematically collected data from women who have had this procedure. Subsequent data revealed that a mean of 14.5 years after surgery, most, but not all, women are satisfied with prophylactic mastectomy and would choose it again. The majority of women also reported a diminished concern about developing breast cancer and favorable effects or no change in self-esteem, satisfaction with body appearance, feelings of femininity, sexual relationships, level of stress in life, and overall emotional stability.[15] However, a substantive minority, 19% of these patients, were negative in their response to their satisfaction, which emphasizes the individuality of results. These data provide women valuable information for making a major, irreversible decision that efficacy information or anecdotal reports alone cannot provide.

Similarly, the efficacy of 2 treatments for localized prostate cancer, either radical prostatectomy or radiation therapy, has shown similar results in terms of survival. QOL outcomes are markedly different for each of these clinical procedures.[16] Significantly more men who undergo the surgical procedure experience urinary and sexual dysfunction (20% and 40%, respectively) than those who undergo radiation therapy.[17-20]

Given these examples, how many individuals would want to make these types of decisions about treatment without knowledge of what others experienced in terms of QOL outcomes? When making decisions on which treatment to choose, a very important issue is knowing the efficacy and mortality data associated with a given treatment or intervention as well as the expected impact of the intervention or treatment on QOL. These data are important for patients to feel they truly are making an informed decision.

QOL: A Softer Measure Than Physiologic Measures?

Why is QOL considered a softer measure than tumor response? In the past, this perception had some validity because it was based on the lag in the development of quantitative instruments and solid research approaches to obtain QOL data compounded by a lack of conceptual refinement for many QOL variables. However, recent work in this field has resulted in tremendous growth and improvement, and the previously held assumptions are no longer valid. Current research indicates that many QOL variables are connected with well-established instruments that have demonstrated reliability and validity. This is certainly the case for variables such as anxiety,[21] depression,[22] mood states,[23] and hope,[24] as well as others. Simple assessment tools are available for measuring global QOL and its various components.[25-27] Additionally, the increased availability of funding for QOL studies has allowed study designs that include samples sizes large enough to have power to detect differences as well as to carry out the study design.

Despite all of these changes and available data, QOL research continues to be referred to as soft science for a variety of reasons. One reason is that physiologic data has traditionally been considered the gold standard, or primary outcome, of importance, with the hard end point being alleviation or stabilization of the specific disease. A second reason is the focus on technology in providing hard end points or factual data.

A final, simple explanation has to do with the relative infancy of QOL assessment as a routine part of clinical practice. About 100 years ago, the routine assessment of blood pressure was a novel idea, and the mechanisms of measurement were largely unknown.[28] Indeed, the veracity of the soft blood pressure cuff readings was

tested via experimentation involving massage therapy, which was considered a known method of reducing blood pressure. The irony inherent is that clinical trials are under way today to assess the impact of massage therapy, with the blood pressure cuff being used to assess the efficacy of massage therapy.[29] The message is that today's soft end point may well turn out to be tomorrow's gold standard.

The relative softness of QOL compared to hard end points, such as tumor response, is a point of discussion. Numerous authors have demonstrated that the relationship between survival and tumor response is weak to moderate.[30] Sloan and Varricchio[31] argued that the rigor with which QOL end points are being measured is actually equivalent to or perhaps superior to that which is being applied to surrogate end point biomarkers.

Healthcare is changing. Patients are demanding that QOL be considered a primary outcome of their care, and research is increasingly demonstrating the importance of QOL end points. QOL has an additional scientific advantage that other end points lack. A patient is unable to assess the relative efficacy of a specific cancer treatment, except in the broadest sense, because there is no proxy for clinical expertise. A clinician, however, is able to provide a proxy rating of a patient's QOL. Recent evidence has suggested that although differences do exist between patient and clinician QOL assessments, consistency is sufficient enough to use one as a surrogate for the other. In general, concordance is better for physical domains than psychosocial domains.[32-35]

Thus, the science behind QOL is strong. Theoretical perspectives and measurements of many select aspects of QOL are refined. Patients understand the importance of QOL as a hard end point. Healthcare professionals can now easily integrate the measurement and use of QOL data in the clinical setting.

Importance of QOL and Symptoms in Relation to Health Outcomes

Symptoms and QOL measures have been shown to be significantly related to adverse physical outcomes, progression of disease, and tumor response. Although the relationship between symptoms and physical outcomes appear readily apparent, the connection between QOL and outcomes appear less evident on the surface. However, an entire science, psychoimmunology, has been developed on the basis of how physiological and psychological outcomes are connected. Several studies have demonstrated the intercorrelation of the physiological and psychological data while providing independent variance of each of these concepts.[36,37]

Quality of Life

QOL data have been shown to contribute an independent explanation of health outcomes beyond that of physiological data. In a study of 112 patients newly diagnosed with biopsy-proven colorectal carcinoma, several aspects of QOL, as measured by proven tools, were significantly correlated with complications after surgery; social function and general health perception (as measured by the Medical Outcomes Study 36-Item Short-Form Health Survey [SF-36]), and social/family, emotional and functional well-being, and cancer concerns (as measured by the Functional Assessment of Cancer Therapy-Colorectal [FACT-C]). Even when these variables were entered into a model including albumin, tumor location, and American Surgical Association tumor stage/classification class, social function and colorectal cancer concerns continued to hold significant associations with complications.[38]

A study of 347 individuals with a myocardial infarction revealed that emotional distress immediately following myocardial infarction was a predictor of poor physical outcomes 1 year later. Anxiety and depression at the time of myocardial infarction predicted subsequent reports of chest pain and everyday activity level. While anxiety and depression did not predict mortality in this study, this may in part be related to the few people who were identified as distressed (15%).[39] A review of studies demonstrates associations between overall poor QOL and job stress, depression,

anxiety, hostility, anger, life events, poor cardiovascular health, morbidity, and mortality.[40]

Although the association can be made between QOL measures and subsequent physical outcomes, physical consequences and disabilities alone do not explain an individual's QOL. In a study of 77 adults with muscular dystrophy, greater disability only partially explained lower QOL as measured by the Quality of Life Profile (r =0.30-0.54).[41] QOL scores were not significantly associated with lung function parameters in a study of 56 lung cancer patients who participated in an inpatient rehabilitation program.[42]

The importance of QOL in relation to adverse effects and health outcomes should not be underestimated. QOL plays a role in predicting health outcomes that are independent of physiologic predictors. Likewise, QOL is not explained by physical measures alone.

Symptoms

Symptom improvement has demonstrated an association with survival that is independent of tumor response. Thus, in trials that show no difference in treatment outcome, symptom improvement may be an important end point in itself. In 1 clinical trial, docetaxel plus cisplatin, docetaxel plus carboplatin, and vinorelbine plus cisplatin were compared in patients with advanced non–small-cell lung cancer. No median survival difference was found when comparing docetaxel plus carboplatin to vinorelbine plus cisplatin, although QOL differed between treatment groups. Although the vinorelbine plus cisplatin arm did not reveal any significant improvements in QOL, the docetaxel plus cisplatin arm demonstrated significant improvements in global QOL, pain control, and weight loss when compared with the vinorelbine plus cisplatin arm. Likewise, the docetaxel plus carboplatin arm demonstrated significant improvements in global QOL, weight loss, and physical function when compared with the vinorelbine and cisplatin arm.[43]

In a study of gefitinib treatment of non–small-cell lung cancer, a dose-dependent improvement in symptoms was seen in 37% to 43% of 140 patients. Radiologic tumor response was associated with symptom improvement. Of the patients with a favorable tumor response, 78% also experienced symptom improvement. Additionally, 53% of the patients with stable disease exhibited improvement in symptoms. Those patients who experienced an improvement in symptoms experienced a longer progression-free survival (4.2 months versus 2 months, respectively) and overall survival (progression not reached versus 6.7 months, respectively) than those who did not show symptom improvement.[44]

Thus, symptoms should be examined in addition to tumor response. Given 2 drug regimens in which survival does not differ, examination of symptom relief can be of particular importance.

Conclusion

QOL is not a soft end point, nor is it supported merely by soft science. Current agendas, programs, and policies increasingly focus on not just adding years to life, but also on identifying ways to improve QOL.[45] The tools and methods for assessing patient QOL routinely, efficiently, and accurately have been developed and are evolving. All that is needed now is for sufficient time and experience to be garnered to increase familiarity with QOL assessment. Although QOL is given much verbal support, more needs to be done to improve the actual integration of QOL into clinical care. Measuring QOL in clinical studies is essential to have sound data available to be used by both clinicians and patients to base treatment decisions.

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