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Using Quality of Life Assessment Methods in Patients with Advanced Cancer: a Clinical Perspective

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The incidence of cancer is expected to increase in most European countries by at least 20–30% in the next two decades. This change in incidence, combined with probably small changes in cure rate, will call for an increased effort in palliative oncology. Most patients with advanced malignant diseases have various unpleasant symptoms which are inadequately treated. In assessing patients' symptoms and well being, health-related quality of life (HRQL) should be the primary endpoint. Several HRQL instruments have been found to be valid for use in cancer clinical trials. The EORTC QLQ-C30 is one among several cancer-specific HRQL instruments. The QLQ-C30 is composed of nine multi-item scales and six single item measures. This instrument is developed to be used in conjunction with disease and/or specific modules.

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INTRODUCTION

ALTHOUGH "the war against cancer" has mobilised considerable resources for basic and clinical cancer research, in terms of cure, only minor breakthroughs have been achieved in the last few decades. Indeed, only 50% of all cancer patients can be cured and, for most of these individuals, the most important curative treatment modality will be surgery, since chemotherapy used alone is rarely curative.

The situation is even more discouraging in the light of the projection of a dramatic rise in the incidence of cancer in the coming decades (Figure 1) [1]. A 20–30% absolute increase in cancer incidence is expected in the next 20 years. The surge in the annual number of new cases reflects both changes in the risk of cancer and changes in the size and structure of the population.

The predicted increase in cancer incidence, coupled with an unsatisfactory cure rate that is not likely to improve substantially, calls for a redoubling of efforts in the area of palliative oncology. Most patients with advanced malignant disease suffer from a number of disturbing symptoms, including pain, asthenia, anorexia, nausea and constipation. And, despite the existence of published guidelines for pain management, many cancer patients are still inadequately treated for pain. In fact, according to a recent study, 42% of inpatients and outpatients with cancer pain receive inadequate analgesic therapy [2]. These findings underscore the need for further research into the management of cancer pain and other symptoms of advanced cancer. Education about cancer pain management is likewise crucial, particularly for physicians who work in medical schools and teaching hospitals.

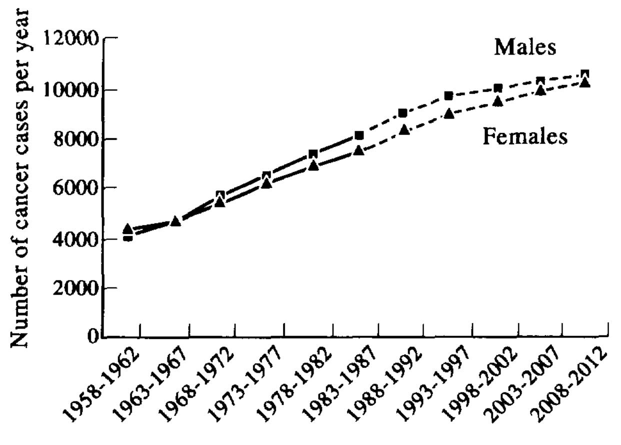

Figure 1. Prediction of cancer incidence in the Nordic countries up to the years 2008–2012. (Adapted from England A, Haldorson T, Tretli S, *et al*. Prediction of cancer incidence in the Nordic countries up to the years 2000 and 2010. A collaborative study of the five Nordic cancer registries. *Acta Pathol Microbiol Immunol Scand* 1993, 38, 101.)

In assessing patient suffering, both in daily clinical practice and in research settings, health-related quality of life (HRQL) should be the primary endpoint. However, in studies of palliative treatment, HRQL is rarely used as an outcome measure [3]. Several factors may account for the paucity of HRQL measurements in cancer clinical trials. First, in striving for improvements in cure rates and long-term survival, most clinicians, and particularly clinical researchers, tend to minimise the importance of improvements in HRQL. This attitude seems to be changing, however, probably because only minor advances have been achieved in the control of cancer. Assessment has also been hampered by limited knowledge of how to measure HRQL and how to organise the infrastructure in clinical trials so as to

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minimise the dropout rate. Finally, another reason for the failure to measure HRQL has been the lack of valid measuring tools.

The last explanation is no longer an obstacle, however. A number of HRQL measuring instruments have been found to be valid for use in cancer clinical trials. These measuring instruments may be categorised either as generic instruments, such as the SF-36, the Sickness Impact Profile (SIP), the Nottingham Health Profile and several others, or as disease-specific instruments. The disease-specific instruments most widely used in oncology today are the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) [4], the Functional Living Index–Cancer (FLI-C) [5], the Cancer Inventory Problem Solving Questionnaire (CIPS) [6] and the Cancer Rehabilitation Evaluation System (CARES) [7].

TREATMENT INTENTION

Before proceeding to a discussion of HRQL measurement in cancer patients, it is important to note that clinicians often do not agree on whether the intention of treatment is curative or palliative. This problem was highlighted in a recent surrogate survey assessing the use of radiation therapy in the treatment of metastatic and locally advanced cancer, which found that physicians who predicted longer survival gave higher doses and more fractionated radiation [8]. Yet another study revealed that oncologists tended to overestimate the therapeutic gain afforded by adjuvant chemotherapy in women with breast cancer [9]. These studies, taken together with clinical experience, suggest that a clear definition and a common international language for treatment intention are needed.

The utility of classifying treatment intention according to predefined categories has been recently assessed in a cross-sectional study of cancer patients in Norway [10]. In this study, treatment intention was categorised as (a) curative, (b) palliative symptom-preventive, or (c) palliative symptom-relieving (Table 1). Study registration took place at all departments of oncology in Norway during a 1-week period. Of the 639 patients studied, 69% received palliative treatment, with an equal distribution between symptom-preventive and symptom-relieving treatment. The proposed definitions were found to be easy to use and provided important information on the number of patients with different cancer diagnoses who were receiving palliative treatment. Our experience in this study has led us to propose a fourth category, life-prolonging treatment, which falls between curative treatment and palliative symptom-preventive treatment. The primary aim here is to prolong survival rather than to cure or to prevent or relieve symptoms.

QUALITY OF LIFE ASSESSMENT

The recognition of how important it is to assess the patient's point of view represents a major step forward in clinical research. Patients are usually the best source of information about their experience of the disease and its treatment. In fact, several studies have shown a discrepancy between quality of life as assessed by health professionals and quality of life as assessed by the patients themselves. These findings are not surprising, since observers can only base their opinions on their own normative standards, which may differ considerably from those of the patient. This does not mean that doctors' or nurses' evaluations of patient HRQL are invalid, but rather that there may be differences based on different life situations. The more life-threatening the disease, the more it alters an individual's life situation and quality of life standards. Therefore, it is commonly agreed that HRQL should be measured by patients themselves.

Table 1. Treatment intention

Curative treatment
The aim of the treatment is to cure the patient of the given disease.
Palliative symptom-preventive treatment
The aim of the treatment is to prevent or delay the onset of a symptom that, with reasonable probability, will arise without treatment. The treatment is directed against the neoplastic tissue.
Palliative symptom-relieving treatment
The aim of the treatment is to alleviate symptoms. The treatment is directed against one or more existing symptoms.

HRQL is multidimensional, encompassing functional status, wellbeing, and general health, including disease-specific and treatment-specific components. All these dimensions can be evaluated with questionnaires. Specially designed, so-called domain-specific instruments can be used to measure psychological, physical, and social functioning. However, the drawback of domain-specific instruments is their length: the patient may have to answer as many as 40–50 questions per domain. For this reason, disease-specific instruments have been created for use in clinical trials.

EORTC QLQ-C36

In 1986, the EORTC began work on a quality of life questionnaire to be used in multinational trials. A modular design was chosen and the first-generation core questionnaire contained 36 questions (EORTC QLQ-C36). A unique advantage of the EORTC QLQ-C36 was that it was cross-culturally developed and tested. In contrast, most of the widely used HRQL measuring instruments and cancer-specific questionnaires have been developed and validated in English-speaking countries.

EORTC QLQ-C30

The EORTC QLQ-C36 was subsequently modified to a 30-item core questionnaire, the EORTC QLQ-C30, which covers general aspects of HRQL. This self-administered questionnaire incorporates nine multiple-item scales and six single-item measures, most of which are related to symptoms. Five of the multiple-item scales involve different aspects of patient functioning: physical functioning (five questions), role functioning (two questions), cognitive functioning (two questions), emotional functioning (four questions), and social functioning (two questions). Three of the multiple-item scales address symptoms, such as fatigue (three questions), pain (two questions), and nausea and vomiting (two questions). In addition, a two-item scale addresses global health and quality of life. Within the core questionnaire there are also single items measuring dyspnoea, sleep disturbance, appetite loss, constipation, diarrhoea, and the financial impact of the disease.

The EORTC QLQ-C30 has been tested in non-resectable lung cancer [11], head and neck cancer [12], a heterogeneous cancer population [13], patients receiving palliative radiotherapy [14], and a mixed Canadian population [15]. All these studies validated the psychometric properties of the questionnaire. Furthermore, a recent test/retest study showed correlations ranging from 0.87 to 0.91 for all scales, except the scale for nausea and vomiting, which had a correlation of only 0.63 [16].

The EORTC QLQ-C30 is designed to be supplemented with disease-specific or treatment-specific modules. In order to standardise and ensure the quality of these modules, the EORTC Study Group on Quality of Life has established specific guidelines for module development. The development process consists of four phases. In phase I, relevant issues are generated through a literature search and through interviews with physicians, nurses, and patients. From the list of issues generated in phase I, questions (items) are constructed in phase II for a provisional model. These questions are developed according to specific criteria in order to achieve a format similar to that of the EORTC QLQ-C30. In phase III, the provisional module is pretested according to a multicentre, multinational testing design. A fixed number of patients must complete the provisional module, answer a debriefing questionnaire, and undergo a structured interview. Problems related to each item can thus be identified and questions deleted or added. Finally, in phase IV, a field testing study is carried out on an international sample of cancer patients in order to determine the psychometric properties of the module.

A module for lung cancer had been already published prior to the development of strict guidelines. Modules for head and neck cancer, breast cancer are now ready for field testing in an international patient sample, while modules for palliative care, oesophageal cancer and paediatric cancer are currently in different stages of development.

CONCLUSION

The new generic HRQL measures have proved useful in measuring the various quality of life domains, and patients are generally positive about completing such questionnaires. High compliance rates can be achieved by optimising the organisation of clinical trials. The EORTC QLQ-C30, the multinationally developed cancer-specific questionnaire, is recommended for use in cancer clinical trials within the EORTC.

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