

Measuring the Quality of Life of Patients with Cancer

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Abstract

What is quality of life? Clinical trials have long been dominated by clinically based endpoints, but research has proved that health-related quality of life (HRQoL) can only be captured accurately by patients themselves using patient-reported outcomes (PROs). The United States Food and Drug Administration defines PROs as the measurement of any aspect of a patient's health status that comes directly from the patient, that is, a measurement taken without interpretation of the patient's responses by a physician or anyone else. The EORTC QLQ-C30 is the most widely cancer specific HRQoL questionnaire used for PROs in the world. Developed in 1991 by the EORTC Quality of Life Group, it has been translated into more than 60 languages and has over 40 developed or under development cancer-specific modules. One of the key challenges faced is pooling data and performing meta-analyses of the results of closed trials. The EORTC Patient Reported Outcomes and Behavioural Evidence (PROBE) team is dedicated to the meta-analysis of EORTC randomised clinical trial quality of life results. During the last 5 years, pooled data have revealed important results, such as prognostic indicators of survival, which have informed clinical practice. This research shows how the patient perspective in palliative and curative EORTC trials has been considered of major importance. The inclusion of patient perspective in drug development shows that a more comprehensive HRQoL assessment has taken place over time as better instruments have become available. As clinicians, regulatory bodies and industry acknowledge the value of the patient perspective, we expect that EORTC will continue including HRQoL endpoints where appropriate.

Keywords

EORTC, cancer, quality of life, patient-reported outcomes

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Clinical trials have long been dominated by clinically based endpoints such as overall survival (OS) and progression-free survival (PFS) to measure the effectiveness of a treatment. A 5-year OS rate, for example, indicates the percentage of patients alive after 5 years of treatment or 5 years after they were diagnosed. PFS indicates the length of time during which a patient's disease does not progress. Neither of these endpoints, however, measure a patient's quality of life (QoL), and research has shown that health-related QoL (HRQoL) can only be captured accurately by the patients themselves using patient-reported outcomes (PROs).

Patient-reported Outcomes

The United States Food and Drug Administration (FDA) defines PROs as the measurement of any aspect of patient's health status that comes directly from the patient, i.e. the patient's responses are not interpreted by a physician or anyone else. EORTC QLQ-C30 is the most widely cancer specific HRQoL questionnaire used in the world. Developed in 1991 by the EORTC Quality of Life Group, it is now translated and linguistically validated into more than 60 languages and can be extended with over 40 modules, addressing specific symptoms, treatments or cancer types.

At the EORTC, the Patient Reported Outcomes and Behavioural Evidence (PROBE) team is dedicated to the meta-analysis and pooled analysis of HRQoL results from EORTC randomised clinical trials. The unique value of this project is the ability to evaluate QoL matters across various types

and stages of cancer. However, a large part of the work is standardising the actual data to be able to combine results across different trials. But these efforts are worth their while and have revealed important results that have informed clinical practice. One of these studies showed, for example, that baseline HRQoL is a prognostic indicator for survival.¹

Better Efficacy Does Not Necessarily Mean Improved HRQoL

In EORTC trial 18991, 1,256 patients with stage III melanoma were randomly assigned to be observed, 629 patients, or to receive, 627 patients, pegylated interferon alpha-2b (PEG-IFN- α -2b) following lymphadenectomy. The results showed that adjuvant treatment with PEG-IFN- α -2b had, at 3.8 years median follow-up, a significant, sustained effect on recurrence-free survival (RFS) in these patients.² However, using the EORTC QLQ-C30, it was observed that the HRQoL of the patients in the PEG-IFN- α -2b arm was more impaired.³ Patients in the PEG-IFN- α -2b arm reported lower scores on two functioning scales (social and role functioning) as well as on three symptom scales (appetite loss, fatigue and dyspnoea) than those in the observation arm. These results highlight the importance of considering HRQoL when making treatment decisions.

HRQoL Plays Role in Practice-changing Trials

Results of EORTC trial 22952-26001 demonstrated that whole-brain radiotherapy (WBRT) did not improve OS and also adversely affected

HRQoL. This trial compared WBRT with observation following either surgery or radiosurgery of a limited number of brain metastases in patients with stable solid tumours. Patients who received WBRT reported lower scores for global health status, physical/cognitive functioning and fatigue, and showed that WBRT following surgery or radiosurgery of a limited number of brain metastases may negatively impact HRQoL; observation with close monitoring by MRI instead of WBRT did not harm HRQoL.⁴

Patient-reported Outcomes versus Proxy Assessment – HRQoL Research in a Novel Area

Assessing HRQoL in patients with brain tumours is challenging. As one would imagine, a commonly reported symptom of patients with gliomas is cognitive deficits, and these also hamper adequate reporting of HRQoL by the patient. Exclusion of patients with cognitive deficits from analysis obviously leads to underreporting of such problems as concentration, memory, reading/writing, ... in the evaluation of HRQoL during experimental treatment.

In EORTC trial 26091, a currently open trial assessing the significance of bevacizumab in recurrent grade II and grade III gliomas, two EORTC HRQoL instruments are being used to assess patient QoL through their caregivers or relatives (proxies). The assessments reported by the patients will then be compared with those reported by their proxies. It would be interesting to find out if the proxies can represent patient views and to what extend the two are in agreement. If proxies have a different perspective, the next question would be which reports the more accurate information.

Future Opportunities

The patient's perspective has consistently been considered important in palliative and curative EORTC trials, and recent findings have altered clinical practice and provide data needed to support major recommendations and future improvements. Clinicians, regulatory bodies and industry representatives acknowledge the value of the patient perspective, and the EORTC will continue to include HRQoL endpoints where appropriate.

Meta-analysis of HRQoL data has been proven clinically informative and, despite the challenges of funding HRQoL research and the complexities of pooling data together, EORTC supports the development the new methods of electronic assessment of PROs and storage in the central EORTC database. Such efforts increase the volume of HRQoL dataset and stimulate numerous efficiency comparisons that can inform clinicians, policy makers, health care payers, etc.

A further development that EORTC is pursuing is the use of HRQoL data collection via computer systems instead of the classic paper questionnaires. Such electronic systems would have several advantages, both for the patient (automatic language selection, adaptive display format ...) as well as the researchers (automatic data transfer, real-time updates on compliance ...). In order to have a machine-independent system, EORTC is developing an online version that will run in all common web-browsers and does not require any local software installation. Once validated, this can be extended to handheld devices and to introduce the questionnaires that can be adapted according to the clinical status of the patient or tailored to his/her previous answers.

About the EORTC

The EORTC brings together European cancer clinical research experts from all disciplines for trans-national collaboration.

Both multinational and multidisciplinary, the EORTC Network comprises more than 2,000 collaborators from all disciplines involved in cancer treatment and research in more than 300 hospitals in over 30 countries.

Through translational and clinical research, the EORTC offers an integrated approach to drug development, drug-evaluation programmes and medical practices.

EORTC Headquarters, a unique pan-European independent clinical research infrastructure, is based in Brussels, Belgium, from where its various activities are coordinated and run (visit www.eortc.org). ■

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