



Development of an EORTC disease-specific quality of life questionnaire for use in patients with liver metastases from colorectal cancer

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Abstract

Quality of life (QL) is an important outcome measure within clinical trials. This paper describes the development of a QL module for patients with liver metastases from colorectal cancer (CRC) to supplement the European Organization for Research and Treatment of Cancer (EORTC) core QL questionnaire, the EORTC QLQ-C30. Phases 1–3 of the EORTC QL Group guidelines for developing QL modules were followed. The literature search generated 71 QL issues. Semi-structured interviews with eight health-care professionals and 47 patients from the United Kingdom, France, Germany and Austria reduced the list to 23 issues. Questionnaire items were formulated to be compatible with the EORTC QLQ-C30. The provisional module was further tested in 102 patients resulting in a 21-item module, the QLQ-LMC21 (Liver Metastases Colorectal). A combination of the core questionnaire and the QLQ-LMC21 will provide essential QL information regarding the use of treatments in both the curative and palliative settings.

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1. Introduction

Colorectal cancer (CRC) is a worldwide health problem. In England and Wales, it was the third commonest cause of death due to cancer in the year 2000 being responsible for over 250 deaths per 1 000 000 of the population in that year [1]. Overall, 40–50% of patients with colorectal cancer develop metastatic disease and the liver is often the first site of metastatic disease and may be the only site of spread in 30–40% patients with advanced disease [2]. Treatment options vary depending on the extent of the metastatic disease. Hepatic resec-

tion of isolated colorectal cancer liver metastases may lead to 40–50% five-year survival rates [3]. Patients with liver metastases not suitable for resection may receive chemotherapeutic or local thermal treatments. The aim of treatment of advanced colorectal cancer is to control symptoms, maintain or improve quality of life (QL) and, ultimately, prolong survival. Survival and disease-free survival are the most frequently used outcome measures, although, patient-based measures of outcome (QL and satisfaction with care) are also being used both as primary and secondary endpoints, especially where the mainstay of treatment is palliation.

The most widely used instruments in assessing QL in cancer patients within the context of clinical trials are the European Organization for Research and Treatment of Cancer (EORTC) core QL questionnaire (QLQ-C30) and

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the Functional Assessment of Cancer Therapy-General (FACT-G) [4,5]. These both use a general core questionnaire and may be supplemented by disease-specific modules [6]. Modules for patients with CRC have been published by both groups [7,8]. Although designed for all patients with CRC, because they concentrate on gastrointestinal symptoms and the side-effects of treatment (stoma problems, bowel habits, sexual function), they may be insensitive and irrelevant to patients with CRC receiving treatment aimed at liver metastases. This was suggested at a consensus meeting in 1996 [9] and, in addition, a Cochrane review of palliative chemotherapy for advanced or metastatic CRC was unable to pool QL results because of the lack of use of valid instruments specific to patients with hepatic metastases from CRC [10]. The aim of this study, therefore, was to develop a disease-specific module specifically for patients with hepatic metastases from CRC according to the EORTC guidelines.

2. Patients and methods

2.1. Study design

The development of the provisional module (phases 1–3) was according to the EORTC Quality of Life Group (QLG) published guidelines for questionnaire development (Table 1) [11,12]. The final part of module development (phase 4) consists of psychometric testing and is under preparation. It is not part of this report.

2.2. Subjects

Patients for the interviews carried out in phases 1 and 3 were recruited from six cancer hospitals in Europe. Eligible patients were required: (a) to have been diagnosed with hepatic metastases from colorectal cancer, (b) to have no other concurrent malignancy, (c) to speak and understand the respective language of the questionnaire (d) to give full informed consent. Ethical committee permission was obtained.

2.3. Data analysis

Descriptive statistics were used to analyse results of the interviews in phases 1 and 3. In phase 1, patients and healthcare professionals rated QL issues from 1 'not at all relevant' to 4 'very relevant'.

The mean relevance rating for each issue and number of times it was prioritised for inclusion were calculated. Mean scores of <2.5 for the professionals and <2.0 for the patients were used as cut-off points for deletion of an issue [13].

The scores were considered in conjunction with qualitative analysis of comments made during the interviews.

Table 1

Guidelines for development of an EORTC disease-specific QL module

Phase	Aim	Process
1	Generation of QL issues relevant to the selected group of patients	1. Literature search 2. Semi-structured interviews with healthcare professionals and patients 3. Analysis of qualitative and quantitative data 4. Combination of results from interviews to produce a list of issues
2	Construction of a provisional questionnaire	1. Consultation of the EORTC QLG item database for existing items 2. Construction of new items 3. Translation of provisional questionnaire according to EORTC QLG guidelines
3	Pretesting the questionnaire for acceptability and relevance	1. Patient completion of questionnaire and interview 2. Analysis of quantitative and qualitative data 3. Modification of questionnaire 4. Formal development report reviewed by EORTC QL group
4 ^a	International field testing	Psychometric testing of the reliability, validity and sensitivity of the module

QL, quality of life; EORTC, European Organization for Research and Treatment of Cancer; QLG, Quality of Life Group.

^a Part of a separate study.

In phase 3, mean scores, range and prevalence were calculated. Cut-off points to consider items for deletion were: mean score > 1.5; range > 2 points; prevalence > 30%; rated a priority for inclusion by patients or professionals in phase 1. Items that met two or less of these criteria were considered for deletion in conjunction with qualitative comments made during the interviews. Remarks or difficulties with comprehension of the items due to wording or language were also taken into consideration when deciding on deletion of items.

3. Results

3.1. Phase 1: generation of QL issues

3.1.1. Literature search

Literature searches were performed in four databases: MEDLINE, PSYCHINFO, EMBASE and WEB OF SCIENCE. The search was limited to the English language and the time period of January 1991 to December 2000. Major subject headings were, colorectal cancer, liver metastases, advanced colorectal cancer and QL. These identified 158 articles. Fifty-three articles measured QL as an outcome using a QL questionnaire. There were no psychometrically tested disease-specific questionnaires used in any of these studies. From these 53 articles, a list of 71 potentially relevant QL issues specific to colorectal cancer were produced.

3.1.2. Semi-structured interviews with patients and healthcare professionals

Semi-structured interviews were carried out with eight healthcare providers and 47 patients. The eight healthcare providers consisted of four oncologists, two cancer surgeons, one palliative care consultant and 1 surgical specialist nurse. The sociodemographic and clinical details of the patients are shown in Table 2.

Analysis of the mean scores for the relevance of each issue resulted in deletion of 21 issues with low scores. A further 26 issues were deleted after a meeting with the gastrointestinal EORTC QLG because of overlap with the core QLQ-C30 questionnaire and because of the generality of some issues. From qualitative analysis of discussions during the interviews, three further issues were added and merging of simi-

lar issues deleted a further four issues. These deletions and additions resulted in a list of 23 issues relevant to the QL of patients with hepatic metastases from colorectal cancer (Fig. 1).

3.2. Phase 2: production of the provisional questionnaire

Items (questions addressing QL issues) were constructed from the 23 QL issues. Criteria for construction were: wording of the items to be compatible with the QLQ-C30 response categories and time frame; existing items from other modules to be used where available. The EORTC QLG item database was consulted to use existing items from other questionnaire modules [14]. Where appropriate, these were preferred to new items. Thirteen existing items for the EORTC QLG item bank were used and 10 new items were created (Fig. 1). The provisional module was at this stage reviewed by two members of the EORTC QL Group and subsequently

Table 2
Sociodemographic and clinical details of patients interviewed in phases 1 and 3

	Phase 1 N = 47	Phase 3 N = 102
Mean age (range)/years	63 (40–85)	66 (35–89)
Gender (male/female)	32/15	60/42
Marital status		
Single	0	7
Married	40	75
Separated/divorced/widowed	7	20
Cohabitation status		
Living alone	7	20
Living with family	39	77
Living with other adults	1	5
Education		
Less than compulsory school	5	0
Compulsory school	20	64
Post-compulsory school	9	22
University	8	13
Unknown	5	3
Employment		
Employed (full-time/part-time)	21	31
Homemaker	6	5
Retired	20	60
Unemployed	0	4
Other	0	2
European country		
Austria	5	17
France	14	15
German	11	15
UK	17	55
Treatment group		
Palliative—chemotherapy	19	35
Palliative—post hepatic resection	3	17
Palliative—best supportive care	17	13
Pre, hepatic resection	5	16
Post, hepatic resection	3	21

UK, United Kingdom.

DOMAIN	ISSUES (n = 23)
Eating	<ul style="list-style-type: none"> • Trouble with eating • Early satiety
Pain	<ul style="list-style-type: none"> • Abdominal pain • Abdominal discomfort • Back pain
Fatigue	<ul style="list-style-type: none"> • Desire to be active • Feeling slowed down • Lethargy * • Lack of energy
Relationships	<ul style="list-style-type: none"> • Social contact with friends • Communication • Decreased sexual interest
Psychosocial	<ul style="list-style-type: none"> • Stress • Loss of enjoyment • Own health in the future • Family in the future
Single items	<ul style="list-style-type: none"> • Taste • Tingling hands or feet • Sore mouth • Dry mouth • Fever * • Jaundice • Weight loss

* deleted after phase 3

Fig. 1. List of quality of life (QL) issues relevant to patients with hepatic metastases from colorectal cancer.

translated according to the strict translating guidelines into French and German [15].

3.3. Phase 3: pretesting

Pretesting was performed in 102 patients (Table 2). The 23 items were considered on the basis of the analysis of the data for each item. On the basis of the descriptive statistics and interviews, two items were deleted: 'Have you felt lethargic?' and 'Have you been bothered by fevers or chills?'. Many patients did not understand the word 'lethargic' and when it was explained it was felt there was overlap with the other fatigue issues. The issue 'fevers/chills' scored very poorly.

The resultant questionnaire consisted of 21 items and has been named the EORTC QLQ-LMC21 (Liver Metastases Colorectal). This was reviewed by two members of the EORTC QLQ Module Development Committee.

4. Discussion

The EORTC QLQ-LMC21 has been methodically developed using standard guidelines. It is designed for use with the QLQ-C30 core instrument to assess all major dimensions of health-related QL in patients with hepatic metastases from colorectal cancer. The content of the questionnaire has been derived not only from the published literature, but also from health professionals dealing with these patients and, most importantly, from the patients themselves. It incorporates the experiences of clinicians and patients from four European countries where the disease has a high prevalence and thus will be applicable to cross-cultural studies and trials. The fourth phase of development is currently in preparation and will provide essential information on the psychometric properties of the questionnaire.

As described in the literature search, there have been many studies in the past 10 years that used QL measurement as a primary or secondary endpoint of treatment. The instrument most frequently used was the EORTC QLQ-C30. Since the literature search was carried out, the FACT Group have published the development and validation of a QL questionnaire for patients with hepatobiliary cancer [16]. This addresses similar issues to the QLQ-LMC21, but as with other FACT QL questionnaires, the scoring produces an overall score giving no indication of how the different dimensions of QL are affected by the cancer and its treatment. It is expected that the EORTC QLQ-LMC21 will be able to provide detailed information on the different aspects of QL because it is a multi, dimensional instrument. It may be used in conjunction with the QLQ-C30 in future trials of new and existing treatments for colorectal hepatic metastases. It may also be of value in the longi-

tudinal day-to-day follow-up of patients within individual cancer centres providing valuable information on the effects of the treatments on patients' lives and explain reasons why progress may not be as expected. It is therefore hoped that the use of the EORTC QLQ-LMC21 will improve individual patients' experiences of their illness by helping carers target treatments where they are most needed.

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