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Development of an EORTC disease-specific quality of life module for use in patients with gastric cancer

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Abstract

Quality of life (QL) is an important outcome in clinical trials in oncology. There is currently no valid international QL measure for gastric cancer. This paper describes the development of a QL module for gastric cancer to supplement the European Organization for Research and Treatment of Cancer (EORTC) Quality of life (QLQ-C30) questionnaire. Phases I to III of module development were conducted in the United Kingdom, France, Germany and Spain according to EORTC QL Group guidelines. Twenty relevant QL issues were generated from the literature and interviews with health professionals ($n=24$) and patients ($n=58$). This produced a 24 item provisional module. Further testing in 115 patients resulted in the QLQ-STO22, containing 22 questions, conceptualised into five scales and four single items, related to disease symptoms, treatment side-effects and emotional issues specific to gastric cancer. The use of the QLQ-C30 supplemented by the QLQ-STO22 will provide a comprehensive QL measure for international trials in gastric cancer.

Keywords: Gastric neoplasm; Quality of life; Questionnaire; EORTC QLQ-C30; EORTC QLQ-STO22

1. Introduction

The prognosis for patients with gastric cancer remains depressingly poor in the West. In the United Kingdom 12 000 new diagnoses and 11 000 deaths attributable to the disease are registered each year [1]. Population-based studies have shown overall 5-year survival rates of 5–20%, a figure that has remained stable over the last three decades [2–5]. Adoption of the more aggressive therapeutic approach used by the Japanese, with the introduction of radical lymphadenectomy and adjuvant regimes has not uniformly conferred a convincing survival advantage in the West [6–8].

The importance of quality of life (QL) as a measure of outcome, in addition to traditional endpoints such as survival, disease-free survival time, morbidity and nutritional function, is now widely recognised, having implications for all patients with gastric cancer. After potentially curative treatment debilitating problems with nutrition, fatigue and postprandial symptoms frequently occur. In considering palliative treatment, any benefit in terms of prolonged survival and symptom relief must be weighed against treatment toxicity or reduction in health-related QL.

Clinical trials in gastric cancer that have used QL as one of their major endpoints have utilised a wide range of methods. These range from physician-based measures of nutrition [9] or symptom scores [10], the use of non-validated '*ad hoc*' questionnaires [11–13] to those that incorporated a simple measure of patients' performance

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status [14–16]. More recently, generic QL instruments, such as the Sickness Impact Profile (SIP) or the Spitzer Quality of Life Index have been used [17,18]. Webb and colleagues used the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life questionnaire (QLQ-C30) to measure QL in patients with advanced oesophago-gastric cancer randomised between two different chemotherapy protocols [20]. Despite differences in survival and anti-tumoral response between the protocols, no differences in QL data occurred, except for global scores at 24 weeks. This indicates a potential lack of sensitivity of the EORTC QLQ-C30 and emphasises the need for a questionnaire specific to patients with gastric cancer. To date, there has been no published gastric cancer specific questionnaire that has been validated for use in international trials.

The EORTC QL Group has developed a modular approach to QL assessment in clinical trials [19]. Patients self-complete a core questionnaire, the QLQ-C30, supplemented by additional site- or treatment-specific modules for particular patient subgroups. To ensure that high quality questionnaires will be produced, detailed guidelines for module development have been published [21]. The use of a generic core questionnaire, applicable to all patients with cancer, facilitates cross-study comparisons, whereas the modules increase the sensitivity to detect small, but clinically important, differences in QL.

This study describes the first three phases of the development of a gastric cancer-specific module. Incorporating QL aspects of patients with adenocarcinoma of the stomach, including tumours of the gastro-oesophageal junction, it is designed to be suitable for use in curative and palliative settings, before, during and after any single treatment or combination of treatments. These include total or subtotal gastrectomy, bypass procedures, adjuvant or primary chemotherapy, external beam radiotherapy, and other supportive measures.

Table 1
Phases of development of the EORTC QLQ-STO22

Phase I
Generation of quality of life issues
Literature search
Semi-structured interviews with patients and health professionals
This produces a list of potentially relevant QL issues
Phase II
Construction of a provisional questionnaire
Items worded to synchronise with QLQ-C30 format and time frame
Items worded to be compatible with QLQ-C30 response categories
Suitable items in existing EORTC modules used to provide consistency
Forward and backward translation of the provisional questionnaire
Phase III
Pre-testing the provisional questionnaire for acceptability and relevance
Patients complete the questionnaire and are interviewed
Results analysed according to response prevalence and variance
Formal development report reviewed by the EORTC QL group
Phase IV
International field testing
Psychometric testing of reliability, validity and sensitivity of the module

EORTC, European Organization for Research and Treatment of Cancer; QL, quality of life; QLQ-C30, Quality of life Core questionnaire; QLQ–STO22, quality of life gancer cancer module.

2. Patients and methods

Module development was conducted according to strict EORTC QL Group guidelines in four distinct phases [21]. Each phase is summarised in Table 1. Phase IV, an international validation study, is currently being prepared (EORTC Protocol Number 15001/40003) and will be the subject of a future paper.

3. Results

3.1. Phase I: generation of QL issues

Literature searches were performed in three databases: MEDLINE (1986 to December 1998), PSYCHINFO (1988 to January 1998) and EMBASE (1980 to December 1998) using major subject headings of gastric neoplasms and QL to identify all pertinent issues previously used in studies addressing the outcome of gastric cancer. This identified 51 articles, six of which incorporated '*ad hoc*' gastric cancer-specific questionnaires [11–13,22–24]. Using these instruments and detailed interviews with two gastric cancer surgeons and an oncologist, a list of 42 potentially relevant QL issues was produced.

3.2. Phase I: semi-structured interviews

The list of 42 issues was discussed in semi-structured interviews with 24 health professionals and 58 patients, who were asked to rate each issue with regard to its relevance to a QL questionnaire and to suggest any additional issues. Generic issues found in the EORTC QLQ-C30 were deleted from the list. Relevance was defined by the frequency and amount of trouble caused by each issue. Issues were deleted if 25% or more patients considered them irrelevant [21]. Issues were added if patients or specialists considered them important. The health professionals, 19 from the UK and five from Spain, included 11 gastrointestinal surgeons, four oncologists, one gastroenterologist, two palliative care

consultants, three general practitioners and three specialist nurses. The patients were selected from France, Germany, Spain and the UK to represent a range of disease stages and treatments. The socio-demographic and clinical features are shown in Table 2.

Based on the quantitative results and comments collected from the interviewees, 24 issues were deleted, nine were found to be irrelevant, seven were sufficiently covered by the QLQ-C30 core questionnaire and 14 were combined to form six issues because of content overlap. Some of the issues traditionally thought to be important in dumping syndrome, such as dizziness, fainting or sweating after eating or palpitations, did not meet the criteria for inclusion. Patients who did report postoperative dumping syndrome said that these particular issues should not be included in the questionnaire. They did, however, comment that postprandial discomfort and bloating followed by urgent diarrhoea, were very troublesome. The QLQ-C30 addresses problems with diarrhoea and the other issues were included in the final module. Two further issues were added, dysphagia and acceptance of the diagnosis. This produced a total of 20 issues.

3.3. Phase II: construction of a provisional module, list of items

A list of items, (specific questions addressing QL issues), were constructed from the 20 QL issues. Items were worded to be compatible with the QLQ-C30 response categories and a time-frame of 1 week. Items were constructed according to recognised principles of questionnaire construction. Twenty-four items were formed from 20 issues. The issue of dysphagia required three items to produce a scale addressing problems with swallowing solid, soft and liquid foods. The issue of body image required two items addressing physical attractiveness and satisfaction with bodily appearance. The issue of burden of ill health required two items assessing the burden of illness and the burden of treatment separately. Twenty-one items were similar to items in other EORTC QL modules and three new items were constructed. The provisional module was translated into French, German and Spanish according to the guidelines for questionnaire translation written by the EORTC QL Group [25].

3.4. Phase III: pre-testing of the provisional module

Pre-testing was designed to identify problems with specific items and to ensure the module adequately covered QL experiences in a larger sample of patients. Patients completed the EORTC QLQ-C30, the provisional module, a debriefing questionnaire and then underwent a structured interview. The results were summarised according to response prevalence (range and mean score) and variability. Items with low frequency (mean score <1.5) and/or low variability (range <2) were considered for exclusion. The qualitative results extracted from the patients' interviews were used to help decide which items should be included in the module for larger scale field testing.

Pretesting was performed in 115 patients from France, Germany, Spain and the UK (Table 2). The population, restricted to those with adenocarcinoma, represented the full spectrum of treatment modalities at a wide range of intervals before, during or after treatment. Twenty-seven interviews were conducted before the start of therapy, 42 within 3 months of commencing it, 22 between 3 months and 1 year and 24 at least 1 year after completion. The median time for patient self-completion of both the QLQ-C30 and the provisional gastric module was 11 to 15 min.

Twenty items met the criteria for inclusion, 12 remained unchanged and eight were modified to clarify the meaning. The dysphagia scale did not exclusively

Table 2
Sociodemographic and clinical features of patients in phases I and III

	Phase I ($n=58$) n (%)	Phase III ($n=115$) n (%)
France	21 (36)	11 (10)
Germany	7 (12)	38 (33)
Spain	15 (26)	9 (8)
UK	15 (26)	57 (50)
Age (mean and range)	60.0 years (22–80 years)	65.6 years (35–97 years)
Gender (M:F)	38 (66):20 (34)	75 (65):40 (35)
Primary treatment		
Surgical resection	23 (40)	49 (43)
Surgical resection + chemo-radiotherapy	17 (29)	15 (13)
Primary chemo-radiotherapy	2 (3)	–
Palliative resection or bypass	2 (3)	17 (15)
Palliative chemotherapy	8 (14)	21 (18)
Palliative surgery + chemotherapy	4 (7)	1 (1)
Best supportive care	2 (3)	12 (10)

assess mechanical obstruction to the food bolus, but also dietary restriction due to early satiety or symptoms of gastric outlet obstruction. As there was already a specific item addressing early satiety, the wording of the dysphagia scale was changed to make it more specific. Problems were experienced with the term 'stomach pain', particularly in those patients who had undergone gastrectomy and the wording was changed to 'stomach area' instead.

Four items were deleted: three failed to meet the criteria (burden of the illness or treatment and susceptibility to common infections) and one because of overlap (body dissatisfaction). One additional item, change in the sense of taste, was added to the module. The item referring to hair loss was transformed into two separate items for clarity.

This resulted in a 22 item EORTC gastric cancer module (QLQ-STO22). This module has undergone careful translation into nine European languages [25]. The module is currently conceptualised as consisting of five hypothesised scales and four single items covering disease and treatment-related symptoms and specific emotional consequences of gastric cancer (Table 3). The scaling will not be finalised until completion of the psychometric testing in phase IV. A full report [26] of phases I to III has been peer-reviewed and accepted by the EORTC QL Group. Fig. 1 summarises the phases and time-frame of module development.

Table 3
Contents of the EORTC QLQ-STO22

Multi-item scales
Dysphagia/odynophagia
Eating solid food
Eating soft or liquidised food
Drinking liquids
Discomfort when eating
Pain/discomfort
Pain in stomach area
Discomfort in stomach area
Abdominal bloating
Dietary restrictions
Early satiety
Enjoying meals
Eating slowly
Change in taste
Trouble eating in front of others
Upper gastro-intestinal symptoms
Reflux
Acid indigestion/heartburn
Trouble belching
Specific emotional problems
Thinking about their illness
Worry about weight loss
Worry about future health
Single items
Having a dry mouth
Body image
Hair loss (two questions)

4. Discussion

The EORTC QLQ-STO22 has been developed using standard guidelines to ensure that, when used with the QLQ-C30, it assesses all major dimensions of QL in patients with gastric cancer. The content has been based on the literature, the views of clinicians and on issues defined by 173 patients in four European countries receiving a broad range of treatments.

Health-related QL in gastric cancer has evolved from mathematical formulae [27] to a multi-dimensional concept encompassing all aspects of patients' health; physical and psychological symptoms and the effects of the disease on patients' social and role function. In 1987, Troidl and colleagues [28,29] developed a questionnaire, consisting of symptom and socio-personal

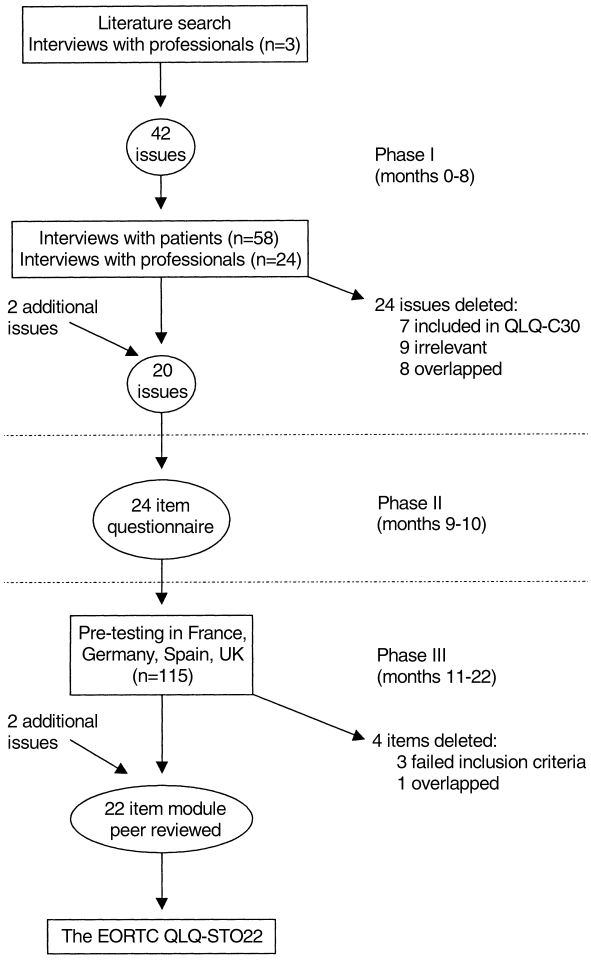

Fig. 1. QLQ-STO22 — phases and time-frame of the development process.

variables. Developed for use in German patients only, formal validation data have not been published. More recently, Thybusch-Bernhardt and coworkers in Kiel University published a gastric cancer-specific questionnaire [30]. This was developed for patients undergoing gastrectomy. Although the authors suggest this questionnaire can be used with the QLQ-C30, the format, style and development of this questionnaire are not consistent with the approach recommended by the EORTC QL Group. It is also not known how this German questionnaire performs in patients with gastric cancer undergoing treatments other than total gastrectomy.

A variety of instruments have been used to measure QL in existing studies, creating difficulties in cross study comparisons. The future of QL assessment in clinical trials lies with standardised instruments with demonstrated reliability and validity that are sensitive to small, but important, changes in disease- and treatment-related QL. The EORTC approach provides sensitive QL measures that allow comparisons across studies performed in multiple international centres.

The rigorous development process, including extensive interviews with patients to establish relevance and a multilingual approach to maximise cross-cultural applicability, ensures that the EORTC QLQ-STO22 is solidly based in the issues that are important to patients with gastric cancer, at every stage of treatment. External peer review and the use of tried and tested standard formats should eliminate difficulties with wording of questions and ensure that the questionnaire is comprehensible to patients and that the responses are easy to evaluate.

The EORTC QLQ-STO22 is now available in nine European languages. It will undergo psychometric examination in an international field study (EORTC protocol number 15001/40003) to ensure it is an appropriate and psychometrically-tested instrument to use in international clinical trials in patients with gastric cancer.

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