PERGAMON

European Journal of Cancer 39 (2003) 1384–1394

European Journal of Cancer

www.ejconline.com

Clinical and psychometric validation of an EORTC questionnaire module, the EORTC QLQ-OES18, to assess quality of life in patients with oesophageal cancer

J.M. Blazeby[a,*], T. Conroy[b], E. Hammerlid[c], P. Fayers[d], O. Sezer[e], M. Koller[f], J. Arraras[g], A. Bottomley[h], C.W. Vickery[a], P.L. Etienne[i], D. Alderson[a]
on behalf of the European Organisation for Research and Treatment of Cancer Gastrointestinal and Quality of Life Groups

[a]*Department of Surgery, University of Bristol, Bristol Royal Infirmary, Bristol BS2 3HW, UK*
[b]*Department of Medical Oncology, Centre Alexis Vautrin, Vandoeuvre-Lès-Nancy, France*
[c]*Department of Otorhinolaryngology Head and Neck Surgery, Sahlgrenska University Hospital, Gõteburg, Sweden*
[d]*Department of Public Health, University of Aberdeen, Aberdeen, UK*
[e]*Department of Oncology and Hematology, Universitätsklinikum Charité, Berlin, Germany*
[f]*Institute of Theoretical Surgery, Philipps-University, Marburg, Germany*
[g]*Hospital De Navarra, Department of Oncology, Irunlarrea, Pamplona, Spain*
[h]*EORTC Quality of Life Unit, EORTC Data Centre, Brussels, Belgium*
[i]*Clinique Armoricaine de Radiologie, Saint Brieux, France*

Received 25 February 2003; accepted 27 February 2003

Abstract

Quality of life (QOL) assessment requires clinically relevant questionnaires that yield accurate data. This study defined measurement properties and the clinical validity of the European Organisation for Research and Treatment of Cancer (EORTC) questionnaire module to assess QOL in oesophageal cancer. The oesophageal module the QLQ-OES24 and core questionnaire, the Quality of Life-Core 30 questionnaire (QLQ-C30) was administered patients undergoing treatment with curative ($n=267$) or palliative intent ($n=224$) and second assessments performed 3 months or 3 weeks later respectively. Psychometric tests examined scales and measurement properties of the module. Questionnaires were well accepted, compliance rates were high and less than 2% of items had missing data. Multi-trait scaling analyses and face validity refined the module to four scales and six single items (QLQ-OES18). Selective scales distinguished between clinically distinct groups of patients and demonstrated treatment-induced changes over time. The EORTC QLQ-OES18 demonstrates good psychometric and clinical validity. It is recommended for use with the core questionnaire, the QLQ-C30, to assess QOL in patients with oesophageal cancer.

Keywords: Quality of life; Oesophageal cancer; Questionnaires; QLQ-OES18; QLQ-C30; Validation; Oesophagectomy; Chemotherapy; Stents

1. Introduction

Potentially curative resection of the oesophagus for oesophageal cancer is associated with significant morbidity and hospital mortality rates of approximately 5%. Long-term survival may be achieved after curative resection. However, most patients present with advanced disease and overall 5 year survival rates are poor [1–2]. Non-surgical treatment with radiation therapy plus chemotherapy is sometimes advocated for patients with squamous cell tumours, but this treatment may have significant complications and has not been widely evaluated in randomised studies [3]. The role of neoadjuvant treatment before surgery remains controversial [4–7]. Endoscopic palliation of malignant dysphagia or palliative chemotherapy may decrease symptoms, but survival benefits are small and sometimes at the expense of treatment-related toxicity [8,9]. The selection of specific treatments can be difficult and is dependent on disease stage, the general health of the

* Corresponding author. Tel.: +44-117-9282336; fax: +44-117-9252736.
E-mail address: j.m.blazeby@bristol.ac.uk (J.M. Blazeby).

0959-8049/03/$ - see front matter © 2003 Elsevier Science Ltd. All rights reserved.
doi:10.1016/S0959-8049(03)00270-3

patient and knowledge of treatment outcomes. Morbidity, mortality and survival data are widely available, but a growing body of opinion considers that a measure of the broader effects of ill health and treatment on the patient's quality of life (QOL) is necessary.

Although there is no strict definition of the elements that contribute to health-related QOL it is generally accepted that they include physical, social and psychological aspects [10,11]. These may be assessed with a valid QOL questionnaire such as the Short Form (SF)-36, Functional Assessment of Cancer Therapy Scale-General Measure (FACT-G), Gastro Intestinal Quality of Life Index (GIQLI) or the European Organisation for Research and Treatment of Cancer Quality of Life Core 30 (EORTC QLQ-C30) [12–15]. Some of these well known instruments have been specifically designed for patients with cancer and they may be supplemented by disease-specific modules to improve coverage, sensitivity and specificity of the core instrument [14,15]. For patients with oesophageal cancer, an additional module to assess important issues such as dysphagia and eating is essential because of their impact on QOL [16]. The EORTC Quality of Life Group has developed a disease-specific module for oesophageal cancer, the QLQ-OES24 based on interviews with patients, health-care professionals and the literature [17]. This questionnaire was designed for use in patients with oesophageal cancer undergoing surgery, chemotherapy, radiotherapy and/or endoscopic treatment. However, its clinical validation or psychometric properties have not been assessed. The aim of this study was therefore to test the reliability and validity of the EORTC oesophageal cancer module in patients undergoing treatment for oesophageal cancer.

2. Patients and methods

This study opened in March 1998 and closed in October 2001. It was co-ordinated at the Quality of Life Unit at the EORTC Data Centre in Brussels (Protocol 15961/40973). Patients were prospectively registered before treatment. Informed consent and local or national ethical committee approval were obtained.

2.1. Patients

Patients with newly diagnosed oesophageal squamous cell or adenocarcinoma were eligible for the study. Patients were staged and selected for treatment according to local policies. Investigators then entered patients into two broad categories for the purpose of questionnaire validation. Categories were formed according to treatment intent. Group A consisted of patients undergoing potentially curative treatment (subgroups, (1) surgery alone, (2) chemotherapy and radiotherapy). Patients were excluded from Group A if they had pre-operative evidence of haematogenous disease spread. Group B included patients receiving treatment with palliative intent (subgroups, (3) endoscopic palliation of dysphagia, (4) palliative chemotherapy and/or radiotherapy). The following exclusion criteria were applied to all patients: life expectancy of less than one month; inability to understand the language of the questionnaire; brain metastases with cognitive impairment; other previous or concurrent malignancies and participation in another QOL study interfering with this protocol. There were no limits on age or performance status. Fig. 1 illustrates the protocol.

2.2. Questionnaires and data collection

Patients completed the EORTC QLQ-C30 (version 3.0), the oesophageal module, QLQ-OES24 and a debriefing questionnaire within four weeks prior to treatment [15,17]. Patients in Group A (curative intent) completed follow-up questionnaires 12 weeks $\pm$ 3 weeks after treatment. Patients in Group B completed the second set of questionnaires 3 weeks after the start of treatment $\pm$ 2 weeks. Patients with QOL assessments outside these time frames were excluded from the data analyses. The follow-up assessment points was selected to test the sensitivity of the questionnaires to *changes* in QOL.

The QLQ-OES24 contains 24 questions (items), in a similar layout and response format to the core questionnaire. The module was translated according to strict EORTC QOL Group guidelines into 13 languages [18]. Responses to the core questionnaire and module were transformed into 0–100 scores, with a high score implying a high level of symptoms or a high level of functioning or global QOL [19]. The module addresses a time frame of 'during the last week'. A debriefing questionnaire records the time required to complete both questionnaires, the need for assistance and the presence of questionnaire items that are considered confusing, difficult to answer or upsetting. The QLQ-C30 contains scales and items addressing functional aspects of QOL and symptoms that commonly occur in patients with cancer. Version 3.0 differs in three respects from Version 1.0: the role functioning and overall QOL scales have changed and the dichotomous response format of the items of the physical and role functioning scale has been replaced by four-point response categories.

2.3. Statistical analyses

A range of analyses was conducted to test empirically the hypothesised scale structure of the QLQ-OES24, investigate scale reliability and evaluate the validity of the questionnaire scales and single items. Analyses were conducted within baseline data sets from both groups and within follow-up data-sets from the four subgroups (Fig. 1). After review of the results and reduction of the

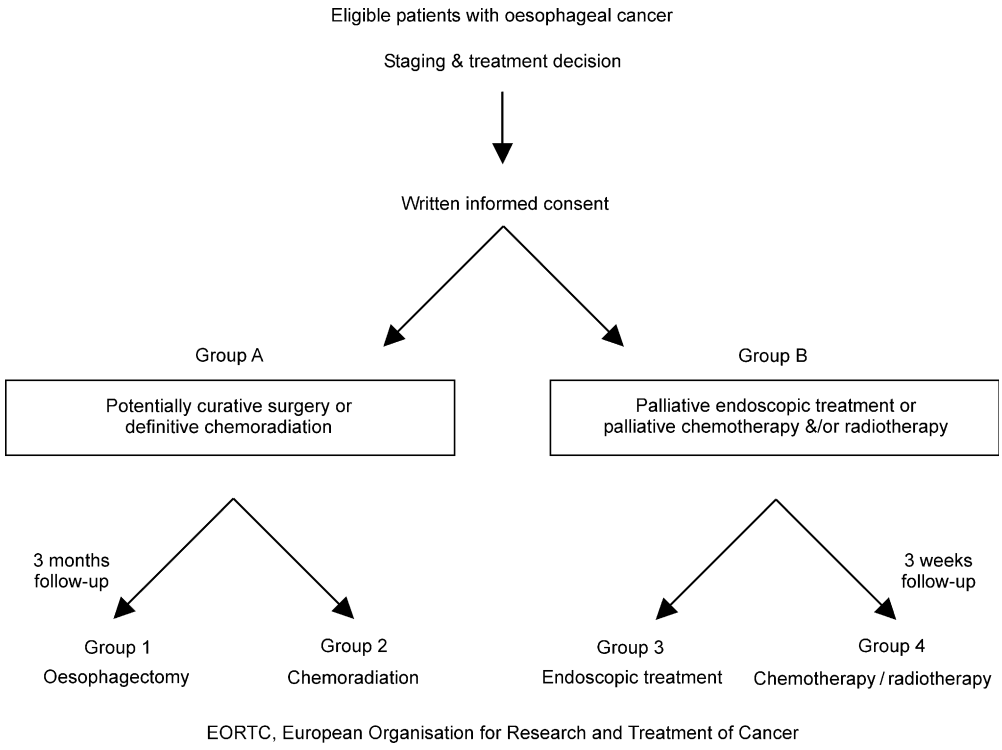

Fig. 1. Patient groups for validation of the EORTC oesophageal module. EORTC, European Organisation for Research and Treatment of Cancer.

module to 18 items, all analyses were repeated to confirm the final scales and establish reliability and validity of the QLQ-OES18 (Fig. 2).

The statistical software program STATA 7 was used for descriptive analyses [20]. MAP software was used for scaling analyses [21]. Tests of differences between groups were performed using unpaired t tests. To protect against problems associated with multiple-significance testing, a conservative P value of <0.01 was regarded as statistically significant.

2.4. Defining QOL scales and items in the oesophageal module

A questionnaire scale is a combination of items (single questions) addressing a QOL theme. The EORTC QLQ-OES24 was conceptualised as containing six hypothesised scales and five single items. Scales assess dysphagia, deglutition (pharyngeal swallowing), eating, reflux, pain and anxiety. Single items include dry mouth, taste, trouble talking, trouble coughing and hair loss. To examine whether the individual items in the oesophageal module could be combined into the hypothesised scales, multi-trait scaling analyses were performed. These examined the extent to which the items correlated with each scale. Evidence of convergent validity was defined as a correlation of >0.40 (corrected for overlap) between an item and its own scale. Item discriminant validity was indicated when an item had a higher correlation with its own scale (corrected for overlap) than with another scale. Items that consistently correlated more highly with another scale than the original one were considered as 'scaling errors'. They were discussed and revisions made. After revising the scales, the psychometric properties of the new scales in the module were re-explored by use of the revised correlations between items and scales, analyses of internal consistency, clinical and construct validity.

2.5. Reliability

Internal consistency refers to the extent to which the items within a scale are interrelated. This was measured with Cronbach's alpha coefficient. Values above 0.7 are generally regarded as acceptable and over 0.8 good [22].

2.6. Validity

The revised scales of the QLQ-OES18 were correlated with scales in the QLQ-C30 to examine the relationship between the disease-specific symptoms and generic aspects of QOL. Scales in the new module would not be expected to relate to generic aspects of QOL unless they addressed similar themes (e.g. pain).

2.7. Clinical validity

Clinical validity of the oesophageal module was assessed in two ways. The extent to which the module was able to discriminate between different groups of

EORTC QLQ – OES18

Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems during the past week. Please answer by circling the number that best applies to you.

During the past week:	Not at all	A little	Quite a bit	Very much
1. Could you eat solid foods?	1	2	3	4
2. Could you eat liquidised or soft foods?	1	2	3	4
3. Could you drink liquids?	1	2	3	4
4. Have you had trouble swallowing your saliva?	1	2	3	4
5. Have you choked when swallowing?	1	2	3	4
6. Have you had trouble enjoying your meals?	1	2	3	4
7. Have you felt full up too quickly?	1	2	3	4
8. Have you had trouble with eating?	1	2	3	4
9. Have you had trouble with eating in front of other people?	1	2	3	4
10. Have you had a dry mouth?	1	2	3	4
11. Have you had problems with your sense of taste?	1	2	3	4
12 Have you had trouble with coughing?	1	2	3	4
13. Have you had trouble with talking?	1	2	3	4
14. Have you had acid indigestion or heartburn?	1	2	3	4
15. Have you had trouble with acid or bile coming into your mouth?	1	2	3	4
16. Have you had pain when you eat?	1	2	3	4
17. Have you had pain in your chest?	1	2	3	4
18. Have you had pain in your stomach?	1	2	3	4

Requests for permission to use the questionnaire may be sent to Dr Andrew Bottomley, Head of the Quality of Life Unit, The EORTC Data Centre, Avenue E Mounier 83, Bte 11, 1200 Brussels, Belgium. abo@eortc.be. The EORTC QLQ-OES18 is currently available in Taiwan Chinese, Danish, Dutch, English, Finnish, French, German, Japanese, Norwegian, Polish, Russian, Spanish and Swedish. There is no charge for academic users to use the questionnaire.

EORTC, European Organisation for Research and Treatment of Cancer

Fig. 2. The oesophageal cancer module. EORTC, European Organisation for Research and Treatment of Cancer.

patients differing in clinical status (known group comparisons) was examined. Mutually exclusive groups were formed on the basis of treatment intent (curative, Group A versus palliative, Group B). The four follow-up subgroups (1–4) were also compared to examine treatment-induced differences in QOL scores (sensitivity to changes over time). Variations in mean scores over time, for scales and items in the QLQ-C30 and oesophageal module were examined in relation to treatment group. Items that were non-responsive and showed small differences between groups and over time were considered for removal.

3. Results

3.1. Patient characteristics

591 patients, from six countries, entered the study and completed baseline questionnaires. One hundred

Table 1
Baseline patient socio-demographic and clinical details

	Treatment group A Curative intent $n=267$	Treatment group B Palliative intent $n=224$
Age (%)		
<50 years	33 (12)	13 (6)
50–59 years	69 (26)	46 (21)
60–69 years	100 (37)	70 (31)
70–79 years	61 (23)	65 (29)
>80 years	4 (1)	30 (13)
Gender (%)		
Male	216 (81)	168 (75)
Co-habitation (%)		
Living alone	50 (19)	66 (29)
Living with family	197 (74)	142 (63)
Living with others	20 (7)	15 (7)
Unknown	0 (0)	1 (<1)
Marital status (%)		
Single	26 (10)	26 (12)
Married	189 (71)	124 (55)
Separated/divorced	52 (19)	73 (33)
Unknown	0 (0)	1 (<1)
Highest level of education (%)		
Less than school	26 (10)	26 (12)
Compulsory school	150 (56)	149 (67)
Post-compulsory school	63 (24)	35 (16)
University level	28 (10)	9 (4)
Unknown	0 (0)	5 (2)
Employment (%)		
Full time	74 (28)	35 (16)
Part time	16 (6)	3 (1)
Homemaker	4 (1)	3 (1)
Unemployed	11 (4)	14 (6)
Retired	157 (59)	164 (73)
Other	5 (2)	4 (2)
Unknown	0 (0)	1 (<1)
Histological diagnosis (%)		
Squamous cell cancer	151 (57)	128 (57)
Adenocarcinoma	112 (42)	86 (38)
Other	4 (1)	9 (4)
Unknown	0 (0)	1 (<1)
Dysphagia grade (%)		
Normal diet	72 (27)	29 (13)
Not all solid food	63 (24)	47 (21)
Only soft food	91 (34)	73 (33)
Only liquids	34 (13)	53 (24)
Complete dysphagia	7 (3)	21 (9)
Unknown	0 (0)	1 (<1)
Karnofsky performance score (%)		
>80	175 (66)	69 (31)
⩽80	91 (34)	153 (68)
Unknown	1 (<1)	2 (<1)
Country (%)		
UK	68 (26)	58 (26)
France	75 (29)	62 (28)
Germany	37 (14)	50 (22)
Sweden	50 (19)	32 (14)
Australia	18 (7)	13 (6)
Spain	15 (6)	7 (3)
Other	4 (1)	2 (<1)

(*continued on next page*)

Table 1 (*continued*)

	Treatment group A Curative intent $n=267$	Treatment group B Palliative intent $n=224$
Treatment subgroup (%)		
Oesophagectomy (1)	95 (36)	0
Curative chemotherapy±radiotherapy (2)	172 (65)	0
Endoscopic palliation (3)	0	96 (43)
Palliative chemotherapy ±radiotherapy (4)	0	128 (57)

UK, United Kingdom.

patients were excluded from the psychometric and clinical analyses because the timing of the QOL assessments was outside the specified time windows of the study. There were 267 patients in Group A and 224 in Group B. Socio-demographic and clinical details are given in Table 1.

3.2. Patient compliance and questionnaire feasibility

All patients completed baseline questionnaires ($n=491$). At the follow-up assessment, 39 patients had died and 20 patients felt too unwell to complete a questionnaire. Of the remaining 432 patients eligible for follow-up questionnaires, 25 (6%) were not obtained, 12 patients refused, 7 were not completed for unknown reasons, 3 were administrative failures, 2 patients declined treatment and questionnaire completion and 1 patient felt that it was a violation of privacy. At the baseline assessment, there were 106 (0.7%) missing items from the QLQ-C30 and 173 (1.5%) missing from the QLQ-OES24. At the follow-up assessment, 111 (0.9%) and 159 (1.7%) items were missing from the QLQ-C30 and QLQ-OES24, respectively. There were significantly more missing responses (10%) to item 21 (assessing treatment burden), than other items in the module.

414 (84%) patients returned a debriefing questionnaire. The average time required to complete the QLQ-C30 and QLQ-OES24 was less than 15 min although 130 patients (31%) required some help. The degree of help required was usually minimal, although the proportion of patients requiring help and the time for completion of the questionnaires increased slightly with age and decreasing performance status (data not shown). In general, items were well accepted and clear to the patients. At the baseline assessment, 53 patients reported that questions were confusing or difficult. 22 patients reported that three or four of items 20 (worry about weight loss), 21 (assessing treatment burden), 22 (assessing illness burden) and 23 (worry about future health) were upsetting.

3.3. Defining QOL scales and items in the oesophageal module

Results of the multi-trait scaling analyses are shown in Table 2. Item scale correlations in the dysphagia (DYS), eating (EAT) and pain (OESPA) scales mostly exceeded 0.40. These scales were therefore retained in their original form. In the hypothesised reflux scale (RFX) of the QLQ-OES24, one item demonstrated poor convergent and discriminant validity (item 14). The mean scores for this item were low in all groups and it was therefore deleted, improving the correlations in the new 2-item scale. Two items of the hypothesised deglutition scale (pharyngeal swallowing) showed poor convergent validity (item 4, trouble swallowing saliva and item 5, choking when swallowing). Both items, however, were considered clinically important and demonstrated significant changes after treatment. They were retained as single items in the final module. The four-item anxiety scale (ANX) showed modest to high correlations within all analyses. Despite these data, it was decided to delete this generic anxiety scale from the oesophageal module because 22 patients reported being upset by these items and because it overlaps with the emotional function scale in the core questionnaire. One single item (assessing hair loss), was also deleted because scores were low and less than 20% of patients responded to this question. The other single items were all retained in their original form.

The final module (QLQ-OES18), therefore, has four scales and six single items (Fig. 2). The remaining results in this paper use the scales and items in the QLQ-OES18.

3.4. Reliability

Cronbach's alpha coefficient was lowest in the reflux and pain scales ranging from 0.58 to 0.71 and highest in the eating and dysphagia scales (Table 2). It was above 0.70 in 60% of all the scales.

3.5. Relationships between the module and core questionnaire

Correlations between scales in the core questionnaire and the module for all patients were examined before and after treatment (Table 3). Patterns of correlations were similar at both assessment points and most scales in the oesophageal module had low correlations with

Table 2
Reliability—item convergent validity and item discriminant validity per patient group

QOL scales	Baseline assessment Curative treatment (Group A) $n=267$				Baseline assessment Palliative treatment (Group B) $n=224$				Follow-up assessment Oesophagectomy (Group 1) $n=78$				Follow-up curative Chemoradiation (Group 2) $n=138$				Follow-up palliative Endoscopy (Group 3) $n=71$				Follow-up palliative Chem/radiotherapy (Group 4) $n=106$			
	Con	Dis	Test	α	Con	Dis	Test	α	Con	Dis	Test	α	Con	Dis	Test	α	Con	Dis	Test	α	Con	Dis	Test	α
OES18																								
DYS	0.54–0.71	0.07–0.46	92	0.75	0.51–0.72	0.01–0.44	92	0.75	0.49–0.52	0.05–0.61	67	0.73	0.58–0.66	0.08–0.50	92	0.78	0.29–0.58	0.09–0.43	50	0.59	0.47–0.74	0.07–0.48	83	0.77
EAT	0.49–0.67	0.16–0.48	94	0.78	0.36–0.64	0.07–0.45	69	0.70	0.32–0.72	0.07–0.63	37	0.75	0.46–0.70	0.07–0.47	81	0.80	0.57–63	0.12–0.48	44	0.75	0.49–0.72	0.20–0.46	56	0.73
RFX	0.41–0.41	0.04–0.32	88	0.58	0.50–0.50	0.07–0.32	100	0.67	0.43–0.43	0.00–0.25	88	0.60	0.56–0.56	0.01–0.36	100	0.71	0.50–0.50	0.03–0.22	100	0.67	0.46–0.46	0.10–0.38	62	0.63
OESPA	0.32–0.57	0.06–0.52	92	0.65	0.37–0.53	0.03–0.39	67	0.61	0.22–0.37	0.04–0.36	8	0.47	0.42–0.49	0.10–0.45	50	0.65	0.51–0.68	0.05–0.47	67	0.76	0.51–0.61	0.17–0.43	67	0.73
OES24																								
DEGL	0.26–0.26	0.07–0.39	33	0.41	0.37–0.37	0.14–0.38	42	0.54	0.39–0.39	0.06–0.37	42	0.56	0.49–0.49	0.14–0.41	75	0.65	0.34–0.34	0.03–0.45	8	0.51	0.35–0.35	0.12–0.48	8	0.52
RFX*	0.36–0.47	0.04–0.48	83	0.60	0.15–0.43	0.07–0.33	56	0.49	0.03–0.36	0.00–0.25	11	0.29	0.24–0.55	0.01–0.41	56	0.58	0.45–0.61	0.04–0.36	78	0.69	0.44–0.51	0.07–0.42	67	0.67
ANX	0.41–0.69	0.05–0.37	92	0.75	0.32–0.58	0.00–0.33	87	0.69	0.47–0.78	0.04–0.48	92	0.84	0.47–0.74	0.02–0.35	75	0.79	0.42–0.67	0.04–0.53	54	0.75	0.56–0.80	0.01–0.52	92	0.83

QOL scales: (DYS = dysphagia, EAT = eating, RFX = new 2-item reflux scale, OESPA = oesophageal pain, DEGL = deglutition, RFX* = hypothesised 3-item reflux scale, ANX = anxiety). Con = the range of item-scale correlations (corrected for overlap), Dis = the range of correlations between an item and other scales. Test = the percentage of cases in which an item correlates significantly higher with its own scale (corrected for overlap) than with other scales. α = Cronbach's alpha coefficient. Chem, chemotherapy; QOL, quality of life.

the QLQ-C30. This indicates that the oesophageal module is assessing clinically succinct aspects of QOL that are not just dependent on general aspects of health (such as physical function). An exception was the oesophageal pain scale (assessing chest and abdominal pain) that moderately correlated with the QLQ-C30 pain scale (assessing overall pain) $r=0.58$. The oesophageal eating scale was also moderately correlated with the social function and fatigue scales in the QLQ-C30 ($r=0.48$ and 0.46 after treatment). Both these moderate associations would be expected because of the expected overlap between difficulties eating and its social consequences.

3.6. Clinical validity

Patients in Groups A and B (clinically distinct groups) reported significantly different QOL scores in several functional and symptoms scales. As expected, patients selected for potentially curative treatment (Group A) scored consistently better scores (Table 4). After treatment, patients selected for oesophagectomy reported a different spectrum of QOL scores to patients completing definitive chemoradiation treatment (Table 4). Three months after oesophagectomy, patients reported significantly poorer social function and more nausea and vomiting than after chemoradiation ($P<0.01$). Patients undergoing primary chemoradiation treatment, however, had more problems with dysphagia than patients undergoing surgery ($P<0.01$). Comparison of QOL data between patients undergoing endoscopic palliation of dysphagia and palliative chemotherapy and/or radiotherapy showed that patients selected for palliative chemotherapy had better physical, role, cognitive and social function, but symptoms scores were similar in both groups.

Changes in QOL scores before and after treatment for each treatment subgroup are shown in Table 5. Three months after oesophagectomy, patients reported significantly worse functional aspects of QOL (physical, social, role and cognitive function) and more problems with fatigue, nausea and vomiting, pain, appetite loss, diarrhoea, dry mouth and loss of taste than before treatment. Patients selected for chemotherapy and radiotherapy with curative intent reported a different spectrum of QOL changes to those who had undergone surgery. Patients had more problems eating after chemoradiation treatment, although dysphagia scores had not changed. Eating difficulties may be related to problems with a dry mouth or pain when eating. Differences were demonstrated in QOL in scores from the module as well as the core questionnaire. In the palliative endoscopic treatment group, only QLQ-C30 physical and role function were significantly worse at follow-up assessment, whereas patients reported significantly better scores

Table 3
Validity—correlations between scales in the QLQ-C30 and oesophageal-specific scales of the QLQ-OES18 for the whole group of patients

QOL scale	PF	RF	EF	CF	SF	QOL	FA	NV	PA	OESDYS	OESEAT	OESRFX	OESPA
PF	–	0.74	0.38	0.49	0.56	0.58	−0.74	−0.29	−0.46	−0.28	−0.40	−0.13	−0.30
RF	0.60	–	0.46	0.49	0.67	0.58	−0.73	−0.38	−0.52	−0.22	−0.42	−0.16	−0.28
EF	0.28	0.34	–	0.57	0.50	0.45	−0.51	−0.41	−0.49	−0.16	−0.45	−0.18	−0.36
CF	0.45	0.42	0.36	–	0.54	0.45	−0.53	−0.32	−0.47	−0.17	−0.39	−0.12	−0.40
SF	0.45	0.65	0.52	0.41	–	0.56	−0.57	−0.37	−0.47	−0.11	−0.49	−0.17	−0.31
QOL	0.49	0.54	0.42	0.38	0.47	–	−0.64	−0.36	0.37	−0.33	−0.49	−0.10	−0.37
FA	−0.70	−0.70	−0.44	−0.45	−0.59	−0.62	–	0.38	0.56	0.29	0.48	0.16	0.37
NV	−0.32	−0.30	−0.26	−0.35	−0.31	−0.32	0.41	–	0.37	0.26	0.43	0.32	0.27
PA	−0.46	−0.49	−0.44	−0.44	−0.45	−0.47	0.57	0.35	–	0.25	0.52	0.17	0.58
OESDYS	−0.27	−0.31	−0.03	−0.19	−0.24	−0.33	0.30	0.31	0.18	–	0.41	0.06	0.24
OESEAT	−0.30	−0.41	−0.31	−0.30	−0.42	−0.37	0.46	0.39	0.37	0.45	–	0.23	0.50
OESRFX	−0.04	−0.13	−0.20	−0.17	−0.13	−0.09	0.07	0.27	0.20	0.05	0.24	–	0.31
OESPA	−0.20	−0.30	−0.37	−0.33	−0.34	−0.31	0.37	0.35	0.59	0.17	0.45	0.31	–

Note: Items in the lower left triangle of the diagonal of dashes represent baseline values; items in the upper right triangle of the diagonal of dashes represent follow-up values. The shaded areas describe correlations between the QLQ-C30 and the QLQ-OES18, whereas unshaded areas are within each questionnaire. Scales QLQ-C30: PF = physical, RF = role, EF = emotional, CF = cognitive, SF = social, QOL = global QOL, FA = fatigue, NV = nausea & vomiting, PA = pain. Scales QLQ-OES18: OESDYS = dysphagia, OESEAT, eating, OESRFX = reflux, OESPA = pain.

Table 4
Validity—known group comparisons of differences in mean scores(standard deviations) of scales and items in the QLQ-C30 and QLQ-OES18

Scales and items	Baseline assessments			Follow-up assessments					
	Curative (Group A) $n=267$	Palliative (Group B) $n=224$	P value (t test)	Surgery (Group 1) $n=78$	Chemoradiation (Group 2) $n=145$	P value (t test)	Endoscopic palliation (Group 3) $n=71$	Chemotherapy/ radiotherapy (Group 4) $n=108$	P value (t test)
Function									
PF	86 (15)	68 (26)	<0.01	67 (21)	71 (23)	0.21	56 (27)	72 (24)	<0.01
RF	78 (28)	60 (37)	<0.01	52 (32)	60 (36)	0.14	44 (36)	65 (34)	<0.01
EF	71 (24)	68 (25)	0.10	71 (24)	73 (25)	0.59	69 (26)	70 (24)	0.78
CF	87 (17)	80 (25)	<0.01	75 (22)	81 (23)	0.08	72 (27)	83 (21)	<0.01
SF	80 (26)	70 (32)	<0.01	53 (32)	71 (32)	<0.01	55 (34)	73 (31)	<0.01
QOL	60 (22)	48 (25)	<0.01	57 (23)	58 (22)	0.58	45 (27)	53 (21)	0.05
Symptom									
FA	28 (23)	47 (30)	<0.01	50 (26)	46 (27)	0.32	56 (30)	48 (28)	0.06
NV	13 (21)	22 (26)	<0.01	24 (22)	15 (24)	<0.01	23 (26)	23 (26)	0.99
PA	22 (25)	33 (30)	<0.01	32 (29)	27 (28)	0.22	37 (32)	29 (29)	0.72
OESDYS	32 (22)	44 (25)	<0.01	26 (23)	38 (30)	<0.01	39 (22)	39 (26)	10.00
OESEAT	40 (28)	48 (28)	<0.01	42 (26)	33 (27)	0.02	38 (25)	35 (24)	0.41
OESRFX	18 (24)	17 (25)	0.52	25 (24)	18 (25)	0.05	18 (27)	18 (24)	0.93
OESPA	26 (23)	28 (25)	0.46	23 (20)	19 (21)	0.15	25 (25)	23 (25)	0.68
OESSV	37 (26)	49 (26)	<0.01	20 (30)	14 (25)	0.08	18 (20)	22 (24)	0.29
OESCH	16 (27)	21 (30)	0.07	19 (29)	12 (22)	0.04	15 (25)	17 (29)	0.50
OESDM	18 (28)	38 (37)	<0.01	33 (34)	25 (31)	0.08	39 (36)	36 (36)	0.62
OESTA	29 (36)	34 (37)	0.19	32 (36)	42 (37)	0.07	32 (35)	45 (35)	0.02
OESCO	16 (25)	23 (31)	<0.01	24 (32)	20 (30)	0.32	19 (28)	23 (32)	0.45
OESSP	10 (24)	15 (26)	0.03	12 (24)	15 (29)	0.45	13 (25)	16 (28)	0.50

QLQ-C30 scales (high score = better function): PF = physical, RF = role, EF = emotional, CF = cognitive, SF = social, QOL = global QOL. QLQ-C30 scales (high score = more symptoms): FA = fatigue, NV = nausea and vomiting, PA = pain. QLQ-OES18 scales (high score = more symptoms): OESDYS = dysphagia, OESEAT, eating, OESRFX = reflux, OESPA = pain. QLQ-OES18 items (high score = more symptoms): OESSV = trouble swallowing saliva, OESCH = choking, OESDM = dry mouth, OESTA = taste, OESCO = cough, OESSP = speech.

for dysphagia and eating than before treatment ($P<0.01$). Patients treated by chemotherapy and/or radiotherapy with palliative intent reported a deterioration in physical function three weeks after treatment and significantly more problems with fatigue, nausea and vomiting and a dry mouth.

4. Discussion

This international validation study tested the EORTC QLQ-C30 and the EORTC QLQ-OES18 in a sample of 491 patients with oesophageal cancer. A combination of results from multi-trait scaling analyses, clinical changes

Table 5
Clinical validity—changes in mean scores over time of scales and items of the QLQ-C30 and QLQ-OES18 by subgroup

	Oesophagectomy (Group 1) $n=78$		P value (t test)	Chemoradiation (Group 2) $n=144$		P value (t test)	Endoscopic palliation (Group 3) $n=71$		P value (t test)	Chemoradiation (Group 4) $n=108$		P value (t test)
	Baseline	Follow-up		Baseline	Follow-up		Baseline	Follow-up		Baseline	Follow-up	
QOL scales												
PF	89	67	<0.01	85	71	<0.01	65	56	<0.01	77	72	<0.01
RF	78	52	<0.01	77	60	<0.01	54	46	<0.01	73	65	0.06
EF	72	71	0.81	71	73	0.30	71	70	0.59	70	70	0.80
CF	87	75	<0.01	87	81	<0.01	77	72	0.07	84	83	0.37
SF	79	53	<0.01	79	71	<0.01	66	56	0.02	78	73	0.12
QOL	67	57	<0.01	57	58	0.65	45	46	0.81	55	53	0.23
Symptoms												
FA	11	50	<0.01	30	46	<0.01	66	56	0.13	36	48	<0. 01
NV	20	24	<0.01	14	15	0.63	27	23	0.32	15	23	<0.01
PA	12	32	<0.01	23	27	0.08	30	37	0.09	27	29	0.43
OESDYS	26	26	0.97	39	38	0.57	56	39	<0.01	40	39	0.89
OESEAT	36	42	0.17	40	33	<0.01	56	41	<0.01	40	38	0.46
OESRFX	22	25	0.49	16	18	0.36	12	18	0.13	20	18	0.39
OESPA	25	23	0.41	26	19	<0.01	27	25	0.38	24	23	0.64
OESSV	17	21	0.47	18	13	0.12	31	19	0.02	25	26	0.88
OESCH	13	19	0.12	17	12	0.05	25	15	0.01	19	17	0.48
OESDM	19	33	<0.01	17	25	<0.01	43	39	0.44	25	36	<0.01
OESTA	17	33	<0.01	37	42	0.13	28	32	0.45	40	45	0.14
OESCO	14	25	0.01	16	20	0.11	26	19	0.09	20	23	0.44
OESSP	6	13	0.05	11	15	0.14	13	13	0.75	13	16	0.22

QLQ-C30 scales (high score = better function): PF = physical, RF = role, EF = emotional, CF = cognitive, SF = social, QOL = global QOL, QLQ-C30 scales (high score = more symptoms): FA = fatigue, NV = nausea & vomiting, PA = pain. QLQ-OES18 scales (high score = more symptoms): OESDYS = dysphagia, OESEAT, eating, OESRFX = reflux, OESPA = pain. QLQ-OES18 items (high score = more symptoms): OESSV = trouble swallowing saliva, OESCH = choking, OESDM = dry mouth, OESTA = taste, OESCO = cough, OESSP = speech.

over time and clinical judgement led to revision of the hypothesised scales and the removal of two single items. The final module scale structure (QLQ-OES18) was examined before and after oesophagectomy, radical chemoradiation therapy, endoscopic palliation of dysphagia and palliative chemotherapy and/or radiotherapy. Repeat analyses confirmed four scales (dysphagia, eating, reflux and pain) and six single items: swallowing saliva, choking when swallowing, dry mouth, taste problems, coughing and speech problems. The new scales demonstrated moderate to good reliability and discriminant validity. The module and core questionnaire were sensitive to clinical changes in health over time and were able to discriminate between clinically distinct groups of patients. The questionnaires were well received by the patients, 75% (310/141) completed both instruments within 15 min and less than 2% (279/26,514) of data were missing. The QLQ-C30 and QLQ-OES18 can therefore be recommended as clinically and psychometrically valid instruments to assess QOL in patients with oesophageal cancer.

Measurement of QOL in patients with oesophageal cancer is becoming an important outcome in clinical trials because of the increasing emphasis on patient-based outcome assessment [23]. There have been a few prospective studies assessing QOL after surgery or endoscopic treatment using generic measures of QOL and validated disease-specific questionnaires have rarely been used to prospectively evaluate changes in QOL [8,24–27]. This study shows that after treatment many aspects of QOL have deteriorated (using the core measure), but the disease-specific module demonstrates benefits of treatment (such as relief of dysphagia after endoscopic palliation). This demonstrates the clinical use of using both a core QOL questionnaire and a disease-specific module. The only other disease-specific measure that has been developed for patients with oesophageal cancer is the FACT-E to accompany the FACIT-G measurement system [28]. This has a similar content to the QLQ-OES18, although no psychometric data have been published. The main difference between the QLQ-OES18 and FACT-E (FACT oesophageal module) is the scoring system. An overall FACT-E score is produced from all items, whereas the QLQ-OES18 yields scores for each scale and single item. This approach loses the multi-dimensionality of QOL assessment that may be more useful for clinicians to direct therapy.

Despite this large study in an international sample of patients, this work has some limitations. The numbers within each country are insufficient to examine properly psychometric cross-cultural differences. The study was unable to include nearly 20% (100/591) of the patients initially entered into the database. Patients were exclu-

ded because QOL assessments were performed more than four weeks either before or after the start of treatment or because follow-up assessments were performed outside of the specified time frames of the study. Although this strict approach reduced the sample size, it was considered clinically important to use data from homogenous samples of patients. This study has not examined the measurement properties of the new oesophageal module in patients with benign oesophageal disease or in a healthy control population. In the normal population, symptom scores for dysphagia, abdominal pain and eating problems are likely to be very low. However, further validation of the module would be gained by testing its discriminant validity in patients with gastro-oesophageal reflux disease. One potential weakness of the questionnaire are that internal consistency scores (measured with Cronbach's alpha coefficients) are less than 0.70 reported in 42% of the scales of the QLQ-OES18. These findings may be interpreted in a number of ways and whether the items are considered as indicator or causal variables of QOL. However, the scales have been retained in their present forms, as for clinical reasons the items should be grouped together and also because they demonstrated sensitivity to changes over time.

The EORTC QLQ-OES18 has been developed according to formal procedures specified by the EORTC QOL Group. It has undergone prospective, international psychometric testing in a large group of patients. The results confirm the revised scale structure, reliability and validity of the module. The site-specific module is able to detect treatment benefit (relief of dysphagia) and it is the only QOL questionnaire for patients with oesophageal cancer that has undergone such extensive testing. The QLQ-OES18 is therefore a suitable measure to use with the QLQ-C30 to assess QOL in patients with oesophageal cancer undergoing any single or combination of treatments including: oesophagectomy, chemoradiation, endoscopic palliation or palliative chemotherapy and/or radiotherapy.

Acknowledgements

We thank the following participating centres for entering patients into this study. Universitätsklinikum Charité Campus Mitte, Germany (V. Budach, H. Lochs, J.M. Müller, K. Possinger,), Charité Campus Virchow, Germany (R. Felix, B. Wiedenmann), Bristol Royal Infirmary, Bristol, UK (C.P. Barham, J. Vickers), University Hospital, Colmar, France (F. Husseini), University Hospital, Geneva, Switzerland (A. Roth), University Hospital Charles Nicolle, Rouen, France (B. Paillot), Universitatsklinikum, Charite, Berlin, Germany (P.M. Schlag), Institute of Theoretical Surgery, Philipps-University, Marburg, Germany (H. Klauss, K. Buscher), Sir Charles Gairdner Hospital, Nedlands, Australia (N. Spry) and The Geelong Hospital, Geelong, Victoria, Australia (R. Bell). We also thank Irina Ghislain for help with data management. J.M.B. is a UK Medical Research Council Clinician Scientist. O.S. was supported by a research grant from the Hector Stiftung Weinheim, Germany. J.M.B. was the overall study co-ordinator for the development of the oesophageal module. She was also responsible for co-ordination of the study in Bristol (with C.W.V. and D.A.). T.C., E.H., O.S., J.A. and M.K. have been active in the module development process and were the institutional co-ordinators responsible for recruiting patients in Nancy (T.C.), Gõteborg (E.H.), Berlin (O.S.), Pamplona (J.A.) and Marburg (M.K.). P.L.E. was responsible for the study in Saint Brieux, France. A.B. is the Head of the EORTC Quality of Life Unit in Brussels (responsible for data collection). P.F. provided statistical expertise for the study. All co-authors were involved in editing the final article.

References

1. Akiyama H, Tsurumaru M, Udagawa H, Kajiyama Y. Oesophageal cancer. *Curr Probl Surg* 1997, **34**, 765–834.
2. Hulscher JB, van Sandick JW, de Boer AG, *et al*. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the esophagus. *N Engl J Med* 2002, **347**, 1662–1669.
3. Herskovic A, Martz K, Al Sarraf M, *et al*. Combined chemotherapy and radiotherapy compared with radiotherapy alone in patients with cancer of the oesophagus. *N Engl J Med* 1992, **326**, 1593–1598.
4. Kelsen DP, Ginsberg R, Pajak TF, *et al*. Chemotherapy followed by surgery compared with surgery alone for localised oesophageal cancer. *N Engl J Med* 1998, **339**, 1979–1984.
5. Urba SG, Orringer MB, Turrisi A, Iannettoni M, Forastiere A, Strawderman M. Randomized trial of preoperative chemoradiation versus surgery alone in patients with locoregional esophageal carcinoma. *J Clin Oncol* 2001, **19**, 305–313.
6. Bosset JF, Gignoux M, Triboulet JP, *et al*. Chemoradiotherapy followed by surgery compared with surgery alone in squamous cell cancer of the oesophagus. *N Engl J Med* 1997, **337**, 161–167.
7. The Medical Research Council. Surgical resection with or without preoperative chemotherapy in oesophageal cancer: a randomised controlled trial. *Lancet* 2002, **359**, 1727–1733.
8. Webb A, Cunningham D, Scarffe JH, *et al*. Randomised trial comparing epirubicin, cisplatin and fluorouracil versus fluorouracil, doxorubicin and methrotrexate in advanced oesophagogastric cancer. *J Clin Oncol* 1997, **15**, 261–267.
9. Bleiberg H, Conroy T, Paillot B, *et al*. Randomised phase II study of cisplatin and 5-fluorouracil (5-FU) versus cisplatin alone in advanced squamous cell oesophageal cancer. *Eur J Cancer* 1997, **33**, 1216–1220.
10. Fallowfield L. *The Quality of Life—The Missing Measurement in Health Care*. London, Souvenir Press (E & A) Ltd, 1990.
11. Troidl H. Quality of life: definition, conceptualization and implications—a surgeon's view. *Theor Surg* 1991, **6**, 138–142.
12. Ware JE, Sherbourne CD. The MOS 36-item short-form health profile: subjective health status and medical consultations. *Medical Care* 1992, **30**, 473–483.

13. Eypasch E, Williams JI, Wood-Dauphinee S, *et al*. Gastrointestinal quality of life index: development, validation and application of a new instrument. *British Journal of Surgery* 1995, **82**, 216–222.
14. Cella DF, Tulsky DS, Gray G, *et al*. The Functional Assessment of Cancer Therapy Scale: development and validation of the general measure. *J Clin Oncol* 1993, **11**, 570–579.
15. Aaronson NK, Ahmedzai S, Bergman B, *et al*. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality of life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993, **85**, 365–376.
16. Blazeby JM, Williams MH, Brookes ST, Alderson D, Farndon JR. Quality of life measurement in patients with oesophageal cancer. *Gut* 1995, **37**, 505–508.
17. Blazeby JM, Alderson D, Winstone K, *et al*. Development of a EORTC questionnaire module to be used in quality of life assessment for patients with oesophageal cancer. *Eur J Cancer* 1996, **32**, 1912–1917.
18. Cull A, Sprangers MAG, Aaronson NK, on behalf of the EORTC Quality of Life Study Group. European Organisation for Research and Treatment of Cancer quality of life study group translation procedure. Internal report of the EORTC Study Group on Quality of Life, 1994.
19. Fayers P, Aaronson NK, Bjordal K, Groenvold M, Curran D, Bottomley A. *EORTC QLQ-C30 Scoring Manual*, 3rd Edn. 2001.
20. StataCorp Release 7.0. College Station, TX, Stata Statistical Software, 2001.
21. Hays RD, Hayashi T, Carson S, *et al*. *User's Guide for the Multitrait Analysis Program (MAP)*. Santa Monica, C.A. Rand Corporation, 1988.
22. Fayers PM, Machin D. Quality of life: Assessment, Analysis and Interpretation. Chichester, New York, Weinheim, Brisbane, Singapore, Toronto, John Wiley & Sons Ltd, 2000 (404 pp).
23. The American Society of Clinical Oncology. Outcomes of cancer treatment for technology assessment and cancer treatment guidelines. *J Clin Oncol* 1996, **14**, 671–679.
24. Blazeby JM, Farndon JR, Donovan JL, Alderson D. A prospective longitudinal study examining the quality of life of patients with esophageal cancer. *Cancer* 2000, **88**, 1781–1787.
25. Brunelli C, Mosconi P, Boeri P, *et al*. Evaluation of quality of life in patients with malignant dysphagia. *Tumori* 2000, **86**, 134–138.
26. Barr H, Krasner N, Raouf A, Walker RJ. Prospective randomised trial of laser therapy only and laser therapy followed by endoscopic intubation for the palliation of malignant dysphagia. *Gut* 1990, **31**, 252–258.
27. van Knippenberg FCE, Out JJ, Tilanus HW, *et al*. Quality of life in patients with resected esophageal cancer. *Social Science and Medicine* 1992, **35**, 139–145.
28. Cella D. *The Functional Assessment with Chronic Illness Manual*. FACIT Manual, 1997.