

A prospective comparison of quality of life measures for patients with esophageal cancer*

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Abstract

Among the most widely used instruments to assess quality of life (QOL) in patients with cancer are the European Organization for Research and Treatment of Cancer core questionnaire (EORTC QLQ-C30) and the Functional Assessment of Chronic Illness Therapy, cancer instrument (FACT-G). This study compared these approaches in patients who had undergone esophagectomy for cancer. The EORTC core questionnaire and esophageal module and the FACT-G and esophageal scale were completed by 57 patients. Missing data, relationships between QOL scales and analyses of patients' preferences were examined. There were 14/2736 (0.5%) missing items from EORTC questionnaires and 45/2565 (1.8%) from FACT instruments ($p < 0.01$). Relationships between corresponding generic EORTC and FACT scales were average to good ($r > 0.57$) except for the social function scale ($r = 0.01$). EORTC symptom scores were moderately correlated with the FACT general scale, but poorly related to the FACT esophageal scale ($r < 0.28$). EORTC swallowing scores were moderately correlated with all FACT scales. The FACT-E and EORTC QLQ-C30 measure assess similar generic aspects of QOL (except social function). EORTC esophageal symptom scores relate poorly to FACT esophageal scales, except for swallowing. Choice of QOL measure after esophagectomy for cancer depends upon outcomes of interest. Future studies will determine which instruments are appropriate in each context.

Key words: EORTC QLQ-C30, EORTC QLQ-OES18, Esophageal neoplasms, FACT-G, Quality of life

Introduction

Assessment of patients' self-reported quality of life (QOL) is increasingly recognized as an important outcome in treatment of esophageal cancer. Accurate measurement using appropriate instruments is therefore essential to provide meaningful data. A number of valid generic QOL questionnaires exist and the European Organization for

Research and Treatment of Cancer (EORTC) QL questionnaire (EORTC QLQ-C30) and the Functional Assessment of Chronic Therapy questionnaire (FACT-G) are among the most widely used cancer specific instruments [1, 2]. Both have international validity and follow a similar concept, with a core questionnaire to assess key aspects of QOL (physical, emotional and social function) and site-specific modules for use in particular patient populations. Despite similarities, recent work comparing instruments has demonstrated distinct differences between the scales in the core instruments. It appears that each approach has specific merits and some of the apparently similar QOL

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scales evaluate different aspects of QOL [3–5]. Choice of generic QOL instrument for a clinical or research trial therefore requires careful scrutiny of item (question) content within each questionnaire.

The EORTC QLQ-C30 and the FACT-G core instruments are generic questionnaires designed for use in patients with cancer. They may be accompanied by site-specific questionnaire modules that increase the sensitivity of the core instrument by addressing issues of relevance to a particular population. Esophageal cancer specific modules are available to use with both systems. The EORTC esophageal module, QLQ-OES18, has completed an international validation study confirming reliability and validity of 18 items [6, 7]. The FACT system combines the FACT-G (general measure) with an esophageal scale (17 items) to produce an esophageal specific tool [8]. The EORTC and FACT esophageal modules focus on similar symptoms and common problems related to esophageal cancer. The main differences between the two approaches are the scoring systems. The FACT system produces summary scores for the general part of the questionnaire and a summary score from the esophageal scale. The

EORTC system produces multiple function and symptom scores from both the core questionnaire and site-specific module. The aim of this study was to compare the EORTC and FACT QOL measurement systems in patients who had undergone either neo-adjuvant chemotherapy and esophagectomy or surgery alone for cancer.

Patients and methods

Patients

The study sample consisted of patients who had undergone either neo-adjuvant chemotherapy followed by surgery or esophagectomy alone for esophageal cancer more than 12 months earlier. Patients treated at Bristol Royal Infirmary gave written informed consent. Patients from Exeter were identified at a patient self-help group, where voluntary participation and verbal consent was obtained. Inclusion criteria were ability to complete questionnaires themselves, English native language and no previous exposure to either of the QOL questionnaires. Participants were informed

Table 1. Symptom content and summary scores for the FACT-E and QLQ-OES18

	Fact-E (version 4)	QLQ-OES18
Number of items	17	18
Symptom assessment		
Dysphagia	4 items	4 items
Choking	1 item	1 item
Dry mouth	1 item	1 item
Pain (chest, abdomen & on eating)	2 items	3 items
Hoarseness	1 item	–
Appetite	1 item	In QLQ-C30
Dyspnoea	1 item	In QLQ-C30
Cough	1 (night time)	1 item
Taste	–	1 item
Early satiety	1 item	1 item
Reflux symptoms	–	2 items
Weight loss	1 item	–
Psychosocial issues		
Communication	1 item	1 item
Eating meals (with others)	1 item	2 items
Enjoyment of eating	1 item	1 item
Scales	Single score	Dysphagia Eating Reflux Pain

about the objectives of the study before being asked to fill out questionnaires and were unaware of the affiliation of the main investigator to either QOL instrument.

Assessment of quality of life

Patients were asked to fill in the EORTC core instrument and esophageal module (QLQ-C30 and QLQ-OES18) and the FACT general measure and esophageal scale [1, 2, 6–8]. Patients were given an envelope with questionnaires in the same sequence and asked to record which questionnaire was completed first and which they preferred.

The questionnaires

The EORTC QLQ-C30 and the FACT core instruments have undergone extensive clinical and psychometric testing described in detail elsewhere. Both have been used in patients with esophageal cancer [9, 10]. The EORTC QLQ-C30 (version 3.0) has five functional scales and nine symptom subscales. The EORTC QLQ-OES18 has four symptom scales and 6 single items [7]. Scoring of all EORTC QOL scales involves a linear transformation to a 0 to a 100 scale [8]. The core questionnaire (FACT-G) has four scales that can be combined to produce a summary score (FACT-G). The site specific, esophageal scale (FACT-E) yields a single esophageal score or it can be combined with FACT-G to make an overall FACT-E score. For the purposes of this study FACT-G, FACT-E and the esophageal FACT scores were transformed by linear conversion of original values to a 0 to 100 scale, analogous to the procedure for the EORTC QLQ-C30. This allowed a common response scale for all questionnaires. Differences between item content, scoring systems and summary QOL scores for the FACT-E and QLQ-OES18 are shown in Table 1.

Data analyses and statistical methods

Missing items were recorded for each questionnaire. The two-tailed-Fisher's exact test was used to compare proportions of missing items in both questionnaires. Missing items were then imputed according to published guidelines [11]. For all FACT and EORTC functional scale scores, higher

scores indicate better QOL or ability to function. For symptom EORTC scales and items, higher scores indicate worse QOL or more symptoms. To check for potential effect of the sequence of application on the response level, the scores of four similar items from the EORTC and FACT questionnaires were compared using Mann–Whitney tests. Differences in scores for those filling out the EORTC questionnaire first were compared with scores for those completing this instrument second. Patient preferences for each questionnaire were estimated as percentage preferences, with 95% confidence intervals. Correlation analyses (Spearman's rank correlation coefficient) were performed between corresponding scales of the core instruments, e.g. EORTC QLQ-C30 physical

Table 2. Sociodemographic and clinical details

	N = 57
Mean age, (\pm standard deviation)	67 years (\pm 9.1)
Gender male/female	39/18
Co-habitants	
Living alone	13
Living with family	31
Living with other adults	13
Marital status	
Single	6
Married	41
Separated/divorced/widowed	9
Unknown	1
Education	
Less than compulsory school	1
Compulsory school	34
Post compulsory school	25
Unknown	2
Employment	
Employed full time	13
Employed part time	2
Unemployed	3
Retired	37
Other	2
Months since surgery (inter-quartile range)	22 (16 – 32)
Previous treatment	
Esophagectomy alone	34
Neoadjuvant treatment + esophagectomy	23
Missing items	
FACT-E (total)	45 (2565)
EORTC QLQ-C30/QLQ-OES18 (total)	14 (2736)

functioning versus FACT-G physical well being. It was not possible to make direct comparisons between EORTC and FACT symptom scores in the esophageal modules, therefore EORTC esophageal symptom scores were correlated with the FACT esophageal score, FACT-G (general score) and the FACT-E score. To minimize problems associated with multiple-significance testing, a p -value of <0.01 was regarded as significant.

Results

Sixty one patients were eligible for the study and 57 (93%) completed both questionnaires. The median time since esophagectomy was 22 months (inter quartile range 16–32 months). Forty-five of 2565 items were missing from the FACT-E and 14 of 2736 items were missing from the EORTC QLQ-C30/QLQ-OES24 questionnaires ($p < 0.01$). Sociodemographic and clinical data are shown in Table 2.

Check for a sequence effect and questionnaire preference

Forty-one patients completed EORTC questionnaires first and 15 completed FACT-E first (one unknown). Median scores for four almost identical single items in both questionnaires were similar irrespective of sequence of questionnaire completion (Table 3). Nine patients stated no preference for either questionnaire and 17 did not answer this question. There were 19 patients who preferred the EORTC system and 12 preferred the FACT-E. Preference rate 33% (21–47%, 95% confidence intervals) for the EORTC system and 21% (11–34%, 95% confidence intervals) for the FACT-E questionnaires.

Comparison between corresponding generic scales of the instruments

Correlation coefficients between similar generic FACT scales and EORTC scales are displayed in

Table 3. Median scores for similar items from both questionnaires after linear transformation to a 0 to 100 scale

Item (questionnaire)	Questionnaire completed first		p -Value
	QLQ (n = 41)	FACT-E (n = 15)	
Nausea			
I have nausea (FACT-G)	12.25	25	0.66
Have you felt nauseated (QLQ-C30)	33	33	0.54
Pain			
I have pain (FACT-G)	25	25	0.75
Have you had pain (QLQ-C30)	33	33	0.12
Dry mouth			
My mouth is dry (FACT-E)	25	25	0.45
Have you had a dry mouth (QLQ-OES18)	33	33	0.92
Choking			
I choke when I swallow (FACT-E)	0	0	0.50
Have you choked when swallowing (QLQ-OES18)	0	0	0.62

Table 4. Spearman rank correlation coefficients between FACT-G and EORTC QLQ-C30 scores (n = 57)

EORTC QLQ-C30	FACT-G				FACT-G
	Physical	Social	Functional	Emotional	
Physical	0.67 ^a	0.04	0.61 ^a	0.46 ^a	0.61 ^a
Social	0.78 ^a	0.01	0.61 ^a	0.49 ^a	0.64 ^a
Role	0.65 ^a	-0.02	0.57 ^a	0.38 ^a	0.55 ^a
Emotion	0.63 ^a	0.12	0.58 ^a	0.64 ^a	0.64 ^a
Global QOL	0.67 ^a	0.35 ^a	0.80 ^a	0.36 ^a	0.76 ^a

^aCorrelation is significant at the 0.01 level.

Table 5. Spearman rank correlation coefficients between FACT and EORTC QLQ symptom scales (n = 57)

EORTC QLQ symptoms scales	FACT esophageal scale	FACT-G general scale	FACT-E total
Nausea & vomiting	0.00	-0.32	-0.27
Pain	0.22	-0.25	-0.08
Fatigue	0.05	-0.68 ^a	-0.48 ^a
Appetite loss	-0.24	-0.35	-0.27
Sleep problems	-0.05	-0.41	-0.34
Constipation	0.17	-0.11	-0.07
Diarrhoea	0.04	-0.24	-0.17
Dyspnoea	0.13	-0.49	-0.40
Dysphagia	-0.44 ^a	-0.41 ^a	-0.39 ^a
Eating	-0.28	-0.47 ^a	-0.36 ^a
Reflux	-0.19	-0.35 ^a	-0.19
Pain	0.04	-0.33	-0.19

^a Correlation is significant at the 0.01 level.

Table 4. Correlations between the physical, role/functional and emotional functioning scales of both instruments were good ($r > 0.57$). The QLQ-C30 global QOL score correlated well with the FACT-G general score ($r = 0.76$). Correlations between the social functioning scale of the FACTG and the EORTC QLQ-C30 were very poor ($r = 0.01$).

Comparison between EORTC symptom and FACT scales

Relationships between FACT esophageal scale, FACT-G (general scale), total FACT-E score and EORTC QLQ symptom scales are shown in Table 5. The highest correlation coefficient between scores from the FACT esophageal scale and symptoms in the EORTC questionnaires was 0.44 (dysphagia). EORTC dysphagia scores were also moderately correlated with FACT-G and Fact-E total scores. Other EORTC symptom scores had poor correlations with the FACT esophageal scale ($r < 0.28$). Correlations between EORTC symptoms scales were generally higher with the FACT general scale.

Discussion

Information about QOL outcomes after treatment for esophageal cancer is important. Potentially curative therapies have significant morbidity and there remains considerable debate about the

appropriateness of aggressive approaches in some patients. Tools used to assess patients' QOL, therefore, must be reliable and valid as well as being capable of addressing relevant clinical domains. This study compared two cancer questionnaires and site-specific modules in patients who had undergone either neo-adjuvant chemotherapy plus esophagectomy or surgery alone for cancer. Correlations between key domains in the core questionnaires were good except for social function. Correlations between EORTC dysphagia scores and all FACT summary scores were moderate but other EORTC symptom scores had poor correlations with the FACT esophageal and FACT-E total score. These data suggest that dysphagia scores are the most relevant symptoms for patients with esophageal cancer. Other EORTC symptom scales do not relate to FACT scales and therefore direct comparisons between instruments is not really possible. Direct comparison of face content of both questionnaires revealed considerable overlap. Both modules address most symptoms that commonly occur after surgery, chemotherapy, radiotherapy or endoscopic treatment of esophageal cancer. Choice of instrument, therefore, depends upon choice of relevant endpoints in any given study – the EORTC system offers multiple specific scales and symptom scores, where as the FACT system produces summary scales.

There is a growing interest in QOL assessment for research purposes and in routine clinical practise [12–14]. Choosing an appropriate

assessment instrument with relevant QOL scales and scoring systems is critical. The EORTC QLQ approach with multiple scale and item scores risks problems of multiple comparisons, but has advantages of producing specific symptom scores. In this study, dysphagia scores were moderately correlated with all FACT summary scales, and other important aspects of QOL were poorly related to overall scores. Treatment of esophageal cancer is frequently aimed at relieving dysphagia as well as prolonging survival and therefore availability of eating and dysphagia scores are valuable in clinical practise and trials in oncology [15]. As such individual measurement of these scales, as recommended by the EORTC QLQ approach to QOL measurement makes clinical sense.

Correlation coefficients were used in this study to explore the relationship between scores in the two questionnaires. Although this provides information about the magnitude of the relationship between scores, it does not provide information about how scores within different systems relate to actual symptoms or QOL issues. Others have used this approach with similar limitations [3, 4]. A study that compares scores from both instruments with simultaneous measurement of symptoms would provide more useful information to interpret the magnitude of the relationship between the both sets of scores.

In this study more patients reported a preference for the EORTC QLQ-C30 instrument than the FACT-E. This was not a significant finding, however, and it may reflect that more patients completed the EORTC questionnaires first, thus biasing this preference. This study did not perform debriefing interviews with patients to explore their views of the types of questions in each instrument. There were significantly more items missing from the FACT questionnaires than from the EORTC QLQ-C30 and esophageal module. This might also be explained by the sequencing effect of the questionnaires, although most of the missing items from the FACT questionnaires were related to the sexual item within the social function scale. It is well recognized that items addressing sexual function will have poor completion rates [16].

The issue of comparability of QOL instruments has been dealt with by other studies using the EORTC QLQ-C30 and FACT-G questionnaires [3–5]. Although the core instruments have con-

siderable overlap, they probably focus on different aspects of QOL, in particular in addressing emotional and social issues in patients with cancer. In the social domain when the instruments are closely looked at it shows that the FACT-G is primarily directed at aspects of social support. In contrast, the items on the social functioning scale of the EORTC QLQ-C30 are relevant to limitations in family and social life caused by physical complaints [5]. Much less is known about how disease specific modules in the FACT and EORTC measurement systems compare. One study comparing FACT-BMT (bone marrow transplant module and FACT-G) with EORTC QLQ-C30 also found that the two instruments could not replace each other in the assessment of QOL and that a direct comparison was likely to be misleading [4]. Direct comparison of the EORTC QLQ-OES18 (esophageal module) and the FACT esophageal scale, shows that the items are very similar but the scoring systems lead to unhelpful summation of symptoms that explains the findings in this study.

The current study shows that the two approaches to assessing QOL in patients with esophageal cancer (EORTC vs FACT) system are not interchangeable. Key domains in the core instruments may have similar titles but they address different QOL issues. The social function scale of the EORTC QLQ-C30 has items that differ in face content to those within the social function scale of the FACT-G. Within the esophageal specific modules, items are very similar but because of the different approaches to scoring, results cannot be easily compared. Choice of instrument therefore depends upon the nature of the individual study and the requirement for detailed specific information. The future use of QOL questionnaires as research tools and their application in clinical practise will probably determine which instruments are appropriate in each context.

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