RESEARCH ARTICLE

Psychometric Analysis of a Persian Version of the European Organization for Research and Treatment of Cancer OG25 Quality of Life Questionnaire in Oesophagogastric Cancer Patients

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Abstract

Background: Health-related quality of life (HRQL) is a fundamental outcome in oncology patients and quality of life (QOL) assessment requires clinically relevant questionnaires. The purpose of this study was translation and definition of measurement properties and the clinical validity of Quality of Life Questionnaire (QLQ) -OG25 module in Persian patients with oesophagus, oesophagogastric junction (OGJ) or gastric cancers. Materials and Methods: The translation procedure followed European Organization for Research and Treatment of Cancer (EORTC) guidelines. Both EORTC QLQ-OG25 and a core questionnaire (EORTC QLQ-C30) were administered to patients with oesophagus (150), OG junction (93) and gastric (32) cancer undergoing multi-modal treatments. Convergent and discriminant validity, Cronbach's alpha coefficient and known-groups comparisons were used to examine reliability and validity. Results: In all, 275 patients (mean age 62 years) completed both questionnaires. Compliance rate was high and the questionnaire module was well accepted. We found good reliability for multi-item subscales of QLQ-OG25 (Cronbach's alpha coefficients 0.76-0.89). About 73% had TNM staging and scales distinguished between clinically distinct groups of patients. However, patients in palliative group experienced compromised functional status and worse treatment-associated symptoms than those in the potentially curative group. Test-retest scores were consistent. Multi-trait scaling analysis demonstrated good convergent and discriminant validity. Conclusions: Overall, the Persian version of QLQ-OG25 demonstrated psychometric and clinical validity that supports its application as a supplement to the original tool (EORTC QLQ-C30) when assessing HRQL in patients with upper-gastrointestinal (GI) cancer both in curative and palliative phases.

Keywords: Health related quality of life - EORTC QLQ-OG25 - psychometric properties - Iran

Asian Pac J Cancer Prev, **15 (6)**, 2739-2745

Introduction

Cancer is the third most common cause of death following cardiovascular disease and accident (Mohebbi et al., 2008; Moradpour and Fatemi, 2013) and gastrointestinal (GI) cancers are the most frequent cancers among males and second to females' breast cancer in Iran (Mohebbi et al., 2011). The epidemiological characteristic of upper GI cancer has markedly changed over recent decades so that oesophageal (Otterstatter et al., 2012; Zhang et al., 2012; Lin et al., 2013) and gastric (Camargo et al., 2011; Dikshit et al., 2011; Lin et al., 2011; Nagini, 2012) cancers have been decreasing in many parts of the world. Although these malignancies remain an important public health problem as the leading cancers in Iran, there were considerable variations in the sub-site of upper GI cancer in different parts of the country (Taghavi et al., 2007; Mohagheghi et al., 2009; Mousavi et al., 2009; Pourshams et al., 2010; Najafi et al., 2011; Sepanlou et al., 2013; Mehrabani et al., 2013). While, Ardabil province in northwest has the highest incidence of gastric cancer (GC) and oesophagogastric junction (OGJC) cancer (Sadjadi et al., 2003), Golestan province in the northeast is an area with the highest incidence of oesophageal cancer (OC) in Iran and worldwide (Kamangar et al., 2007).

Health-related quality of life (HRQL) as a routine outcome measure is being used increasingly in clinical settings (Kiebert et al., 2000; Lee and Chi, 2000; Asadi-Lari et al., 2004; Farooqui et al., 2013), which is ideal for determining the efficacy and impact of cancer care. Robust Quality of Life Questionnaires (QLQ) have been developed and validated in the past decades to measure the HRQL of oesophageal and gastric cancers (Hasegawa and Yoshikawa, 2010). Measuring HRQL in patients with cancer may help health professionals and caregivers to guide clinical decision making, to determine the efficacy and impact of cancer care and to identify the

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most troublesome symptoms and functional problems to alleviate patients to confront better with the disease (Ferrans, 2010), including those with oesophageal cancer (Lin et al., 2012).

The European Organization for Research and treatment of Cancer (EORTC) Quality of Life Group (QLG) has developed a modular approach to HRQL measurement in cancer clinical trials(Aaronson et al., 1993). Generic cancer questionnaire of EORTC QLQ-C30 was supplemented by site-specific modules to increase sensitivity and specificity. EORTC QLG has developed the oesophagogastric (OG) site-specific Questionnaire (EORTC QLQ-OG25) to be used in patients with oesophageal, gastric and oesophagogastric junction cancers (Lagergren et al., 2007). EORTC QLQ-OG25 had been validated in European and Mexican patients, where its reliability and validity had been established for HRQL measurement in patients with oesophageal, gastric and oesophagogastric junction cancers undergoing multimodal treatments and follow up (Lagergren et al., 2007; Onate-Ocana et al., 2012; Tomaszewski et al., 2013). The aim of present study was to examine the psychometric properties of translated version of EORTC QLQ-OG25 in Iranian patients.

Materials and Methods

Patients

This was a cross-sectional study conducted in the Medical Oncology Department of Mashhad University of Medical Sciences (MUMS). A consecutive group of patients with upper GI cancer were recruited into the study during September 2010 to April 2011, from two tertiary referral hospitals, a general hospital and a specific oncology hospital, in Mashhad, northeast of Iran. Participants over 18 years, with a histological diagnosis of adenocarcinoma (ADC) and squamous cell carcinoma (SCC) of OC, GC and OGJC were included and those with concurrent malignancy, physical inability, a psychological or linguistic impairment, those refused to participate were excluded (Esmaili-Hesari et al., 2012). Location of tumour, which was classified as OC, GC and OGJC according to Computed Tomography (CT) Scanning, Magnetic Resonance Imaging (MRI), endoscope findings and histopathology study in patients who underwent surgical resection. Clinical stage was defined according to TNM Staging System of American Joint Committee on Cancer (AJCC)(Edge and Compton, 2010). The research protocol was approved by the ethical committee of IUMS and written informed consent was obtained from all patients' prior enrolment. Two hundred and seventy five patients took part in the study and six patients were excluded from our sample due to predetermined criteria; three patients refused to participate in the study without explanation, one patient had concurrent malignancy (breast cancer), one patient suffered from severe physical impairment (amputation feet) and one patient failed to complete the questionnaire (Esmaili-Hesari et al., 2012).

Translation process

The Persian version of the EORTC QLQ-C30 questionnaire had been previously translated (Montazeri et al., 1999). We followed the guidelines for translation and pilot study of the EORTC QLG (Koller et al., 2007). Forward translators 1 and 2 were bilingual (Persian-English) native speaker of Persian, who independently produced two initial Persian version of QLQ-OG25. The translation coordinator compiled two translations and the team chose the most appropriate words as initial forward translation. The First Intermediary Version (FIV) was given to two bicultural and bilingual native English speakers fluent in Persian who had never seen the original module before. In critical review for changing and new wording the Second Intermediary Version (SIV) of QLQ-OG25 was approved. The Second Intermediary Version was sent to the EORTC QOL Unit in Brussels (Belgium) to seek permission to start the pilot study. Upon approval, the QLQ-OG25 was administered to 14 patients with upper-gastrointestinal cancer to assess the understandability of the tool in the first pilot study and to 12 different patients in the second pilot study to ensure that changes in wording were appropriate. Results from pilot studies and interviews were reflected in the final Persian version. (Figure 1)

Questionnaires and data collection

All participants completed the EORTC QLQ-C30 (version 3.0), EORTC QLQ-OG25 and demographic questionnaires. The QLQ-C30 is a self-report multi-dimensional general cancer-specific questionnaire, which measures the main factors influencing patients' lives (Fayers and Bottomley, 2002). The QLQ-C30 is multidimensional, made up of 30 items with five function domains: physical, role, emotional, cognitive and social and one global health status/HRQL domain; three symptom domains including fatigue, nausea-vomiting, pain, and six single items (Aaronson et al., 1993). The core questionnaire, the EORTC QLQ-C30, is an extensively validated questionnaire, examined in multi-cultural clinical studies (Yun et al., 2004; Hoopman et al., 2006; Alawadhi and Ohaeri, 2010; Cheng et al.,

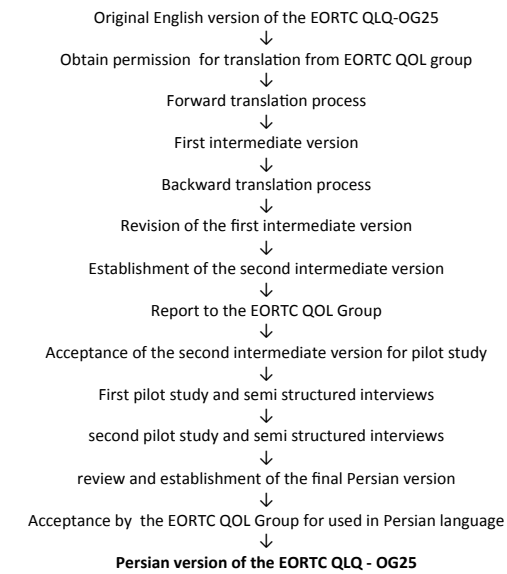

Figure 1. Development of the Persian Version of the EORTC QLQ-OG25

2011; Kontodimopoulos et al., 2012), including Iranian patients (Montazeri et al., 1999). Responses to the core questionnaire and the modules were linearly converted into 0-100 scores using standard EORTC guidelines (Fayers et al., 2001). For the five functional scales and the global QOL scale, a high score means "high level of functioning or global QOL". In case of symptom scales and single item, a higher score implies a "higher level of symptoms or problems"(Fayers et al., 2001).

The QLQ-OG25 is a specific self-report questionnaire designed to assess the HRQL for oesophagogastric cancers. The EORTC QLQ-OG25 contains 25 items in six scales namely dysphagia, eating restrictions, reflux, odynophagia, pain and anxiety and ten single items; eating with others, dry mouth, sense of taste, body image, saliva, choking, cough, speech, weight loss and hair loss. The time frame of the QLQ-OG25 module is the precedent week (Lagergren et al., 2007). The participants also completed a short questionnaire that recorded demographic characteristics and clinical features.

Timing of assessments

We recruited the patients undergoing different treatments modalities consecutively at the out-patient oncology clinics. Participants were instructed to complete the questionnaires themselves and illiterate patients were assisted by relatives or a trained interviewer. Test-retest reliability of the questionnaire was carried out on follow up group since their medical condition was expected to be more stable than those in active treatment, therefore 27 participants in follow up phase were asked to complete a second HRQL assessment between 7-14 days after the first administration of questionnaires.

Statistical analysis

Defining the HRQL scales and items in the QLQ-OG25: questionnaire responses were initially analyzed to establish the scale structure of the QLQ-OG25. Tests of clinical and psychometric validity were performed using the finalized scales and single items. Multi-trait scaling analysis was used to test whether the items of the QLQ-OG25 fitted with the proposed scale structure. Item convergent validity was defined as item-scale correlation of 0.40 or greater and item discriminant validity was indicated when an item had a higher correlation with another scale than with its own scale. Scaling errors were considered to occur when items consistently correlated more highly with another scale or did not correlate with any of the hypothesized scales.

Reliability:Internal consistency and test-retest analysis were performed to examine the reliability. Internal consistency was measured by Cronbach's alpha coefficient with a magnitude over 0.70 being considered acceptable for group comparisons. The test-retest (reproducibility) of the QLQ-OG25 was examined between the first and second test-retest assessments in patients reporting stable health status. Values of ICC vary between zero (totally unreliable) to 1 (perfectly reliable). For stability, reliability coefficient of 0.70 is generally considered acceptable, 0.80 is good, and 0.90 or high is excellent (Lagergren et al., 2007; Onate-Ocana et al., 2012; Tomaszewski et al., 2013).

Validity: convergent validity and clinical validity were conducted to examine scale validity. Correlations between the QLQ-OG25 scales and single items were examined using Pearson's product moment correlation. Pearson's values of greater than 0.40 between an item and its own scale were considered highly correlated as evidence of item convergent validity. It was anticipate that the scales in QLQ-OG25 module would not be expected to relate to generic aspects of HRQL unless they addressed similar themes such as symptom scales (Lagergren et al., 2007; Onate-Ocana et al., 2012; Tomaszewski et al., 2013).

Clinical validity: Known group comparisons examined the extent to which the QLQ-OG25 scores were able to discriminate between subgroups of clinically distinct patients. The clinical parameter hypothesized to form mutually exclusive patient subgroups for comparison included treatment intent (curative and palliative) and tumour stages. It was hypothesized that the patients with lower stage and those in curative group would report better functioning and less symptoms than patients in palliative care. These differences between groups were tested with Chi-square, one way analysis (ANOVA) and student t-test, as appropriate (Lagergren et al., 2007; Onate-Ocana et al., 2012; Tomaszewski et al., 2013).

Results

Patient's socio-demographic and clinical characteristics

In all, 275 patients completed the Persian version

Table 1. Clinical and Socio-Demographic Characteristics of Patients by Tumour Site (n=275)

	OC (N=150)	GC (N=93)	OGJC (N=32)	p value
Gender (%)				
Male	68 (45.3)	67 (72)	24 (75)	<0.001
Female	82 (54.7)	26 (28)	8 (25)	
Age Mean (SD)	63 (11.1)	62 (13.3)	60 (13.3)	
Marital Status (%)				
Married	118 (78.7)	84 (90.3)	25 (78.1)	0.63
Single	0	1 (1.1)	0	
Separate*	32 (21.3)	8 (8.6)	7 (21.9)	
Education (%)				
Illiterate	101 (67.4)	53 (57)	14 (43.8)	0.14
Elementary school	38 (25.3)	29 (31.1)	10 (31.3)	
High school and more	11 (7.3)	11 (11.9)	8 (25)	
Occupation (%)				
Housekeeper	76 (50.7)	23 (24.7)	8 (25)	<0.001
Working	47 (31.3)	44 (47.3)	14 (43.8)	
Retired	3 (2)	14 (15.1)	5 (15.6)	
Unemployed	24 (16)	12 (12.9)	5 (15.6)	
Self care ability (%)				
Yes	97 (64.7)	53 (57)	24 (75)	0.17
Stage of tumor (%)				
I	2 (2.1)	3 (3.7)	1 (4)	<0.001
II	45 (47.4)	10 (12.3)	2 (8)	
III	31 (32.6)	26 (32.1)	8 (32)	
IV	17 (17.9)	43 (51.9)	14 (56)	
Treatment intent (%)				
Curative	108 (72)	42 (45.2)	16 (50)	<0.001
Palliative	42 (28)	51 (54.8)	16 (50)	
Inhabitant status (%)				
Urban	76 (50.7)	49 (52.7)	20 (62.5)	0.48
Rural	74 (49.3)	44 (47.3)	12 (37.5)	

*divorced, widowed; **p value derived from Chi-squared

of QLQ-OG25 questionnaire along with the core questionnaire which was included in the final analysis, which of them 54.6% had oesophageal, 33.8% gastric and 11.6% OGJ cancers. Age ranged from 18 to 89 years with mean of 62 years (SD=11.9). Most of the patients were male (57.8%) and mainly were inhabitant in Khorasan Razavi province (75.6%). About 73% had TNM staging; among them 3% were in stage I, 28.4% in stage II, 32.3% stage III, and 36.3% in stage IV. Clinical and socio-demographic characteristic of patients are shown in Table 1. At interview, time since diagnosis ranged from 2 to 396 months (Mean=15.5, SD=29.6 and median=6 months). All patients completed the questionnaire during a face-to-face interview. The questionnaire was well accepted by the patient population after minor changes resulted from patient's opinion in pilot studies. The majority of patients completed both questionnaires in less than 30 minutes in a calm environment.

Reliability: Cronbach's alpha coefficient ranged from 0.76-0.89 (Table 2). Test-retest scores were consistent and intra-class correlation coefficient (ICC) values ranged from 0.85 for OGDYS scale to 0.98 for OGPD scale for the QLQ-OG25 which indicated acceptable reliability.

Validity:There was a desirable correlation between each item and its own scale leading support to its item-component validity and as shown in Tables 3 and 4 the correlation between an item and its own scale was significantly higher than its correlation with other scales. Correlation between the OG25 module and the QLQ-C30 core questionnaire scales was examined to demonstrate differences and clinical meaning for all patients. Most scales in the QLQ-OG25 were weakly correlated with the QLQ-C30 scales. The dysphagia scale (OGDYS) was moderately correlated with QLQ-C30 fatigue (r=0.50) and eating restrictions scale (OGEAT) was moderately correlated with QLQ-C30 physical function (r=-0.51), role function (r=-0.51), nausea and vomiting (r=0.56), pain (r=0.61), global health (r=-0.53) scales and appetite loss (r=0.64). Likewise, reflux scale was moderately correlated with nausea and vomiting (r=0.51) and anxiety with emotional function scales (r=-0.55). The odynophagia scale was correlated with emotional function (r=-0.54), fatigue (r=0.52) and pain scales (r=0.53). These correlations demonstrate the clinical overlap between the subscales which were expected.

Table 5 summarizes the results of known-group comparisons. We merged patients with stage I and II because of a small number of patients in stage I tumour (n=6). Comparing with patients in higher stages, those with lower tumour stage reported statistically significant higher level of physical and role functioning scales and lower level of fatigue, nausea and vomiting and pain symptom scales in QLQ-C30. All QLQ-OG25 scales demonstrated significant differences ($p<0.01$). Significant difference was detected between curative and palliative groups' scores in functioning and symptom scales of QLQC30 and QLQ OG25 using independent t-test (Table 5). According to tumour site, clinically distinct groups did not demonstrate statistical differences.

Table 2. Mean (SD) and Cronbach's alpha Coefficient QLQ-C30 Scales and QLQ-OG25 Scales

Subscales/Items	Item No	Mean (SD)	Cronbach's α Coefficient
QLQ-C30			
PF	1-5	60(25)	0.87
RF	6-7	63(27)	0.83
EF	21-24	70(21)	0.77
CF	20-25	82(21)	0.68
SF	26-27	52(28)	0.86
FA	10, 12, 18	41(23)	0.77
NV	14-15	27(29)	0.87
PA	9-10	38(25)	0.66
GQL(Global health/ QOL)	29-30	53(25)	0.84
QLQ-OG25			
OGDYS	1-3	29(25)	0.83
OGEAT	4-7	38(24)	0.8
OGREX	8-9	33(29)	0.76
OGODYN	10-11	31(28)	0.84
OGPD	12-13	28(26)	0.83
OGANX	14-15	45(32)	0.89
OGEO	16	30(32)	-
OGDM	17	40(32)	-
OGTA	18	13(24)	-
OGBI	19	26(30)	-
OGSV	20	17(27)	-
OGCH	21	21(26)	-
OGCO	22	25(26)	-
OGSP	23	16(25)	-
OGWL	24	25(31)	-
OGHAIR	25	20(26)	-

*QLQ-C30 functional scales (high score=better function); PF, Physical; RF, role; EF, emotional; CF, cognitive; SF, social; GOL, Global Health Status/QOL; QLQ-C30 symptoms scales (high score=more problems): FA, fatigue; NV, nausea and vomiting; PA, pain; QLQ-OG25 symptom scales and items (high score=more problems): OGDYS, dysphagia; OGEAT, eating restrictions; OGREX, reflux; OGODYN, odynophagia; OGPD, pain and discomfort; OGANX, anxiety; OGEO, Eating with others; OGDM, Dry mouth; OGTA, sense of taste; OGBI, Body image; OGSV, Saliva; OGCH, Choking; OGCO, Cough; OGSP, speech; OGWL, Weight loss; OGHAIR, Hair loss; a- number item in core questionnaire and QLQ-OG25 module

Table 3. EORTC QLQ-OG25; Convergent and Discriminant Validity of Multi item Scales in Subgroups of Patients

OG scales	ALL (n=275)				Oesophagus (n=150)			Stomach (n=93)			O-G Junction (n=32)		
	Item correlation with		ICC	α	Item correlation with		α	Item correlation with		α	Item correlation with		α
	own scale	other scale			own scale	other scale		own scale	other scale		own scale	other scale	
OGDYS	0.464-0.787	0.101-0.659	0.85	0.83	0.455-0.797	0.206-0.658	0.89	0.490-0.772	0.106-0.689	0.79	0.438-0.789	0.049-0.684	0.84
OGEAT	0.426-0.667	0.076-0.525	0.89	0.8	0.455-0.624	0.035-0.567	0.81	0.442-0.655	0.061-0.532	0.8	0.502-0.714	0.139-0.665	0.83
OGREX	0.616	0.162-0.555	0.89	0.76	0.586	0.141-0.529	0.73	0.641	0.179-0.588	0.82	0.67	0.139-0.492	0.77
OGODYN	0.731	0.200-0.594	0.97	0.84	0.772	0.139-0.616	0.91	0.711	0.161-0.668	0.85	0.628	0.235-0.516	0.74
OGPD	0.716	0.073-0.595	0.98	0.83	0.713	0.045-0.616	0.87	0.772	0.012-0.560	0.93	0.736	0.024-0.510	0.84
OGANX	0.808	0.221-0.501	0.97	0.89	0.808	0.187-0.529	0.88	0.78	0.147-0.570	0.89	0.86	0.174-0.559	0.89

*OGDYS, dysphagia; OGEAT, eating restrictions; OGREX, reflux; OGODYN, odynophagia; OGPD, pain and discomfort; OGANX, anxiety; α- Cronbach's alpha Coefficient; a- convergent validity from spearman correlation coefficients; b- discriminant validity from spearman correlation coefficients; c- Intra-class Correlation Coefficient

Table 4. Inter-Item Correlation of HRQL Scales

		OGDYS	OGEAT	OGREX	OGODYN	OGPD	OGANX
Dysphagia	Problem eating solid food	0.85	0.64	0.42	0.49	0.33	0.39
	Problem eating liquidized or soft food	0.93	0.6	0.5	0.53	0.3	0.42
	problem drinking liquids	0.83	0.51	0.46	0.51	0.26	0.42
Eating restriction	trouble enjoying meals	0.52	0.76	0.47	0.52	0.42	0.45
	felt full up after beginning to eat	0.45	0.77	0.46	0.43	0.36	0.43
	taken a long time to complete meals	0.47	0.8	0.42	0.56	0.4	0.41
	difficulty eating	0.68	0.82	0.45	0.58	0.39	0.38
Reflux	acid indigestion or heartburn	0.47	0.5	0.9	0.59	0.48	0.44
	acid or bile problem	0.47	0.53	0.89	0.55	0.45	0.49
Odinophagia	discomfort when eating	0.54	0.65	0.59	0.92	0.55	0.47
	pain when eating	0.54	0.58	0.58	0.93	0.57	0.5
Pain and discomfort	pain in stomach	0.35	0.42	0.45	0.6	0.92	0.35
	discomfort in stomach	0.3	0.49	0.51	0.52	0.93	0.41
Anxiety	thinking about illness	0.43	0.49	0.5	0.47	0.41	0.95
	worry about health in the future	0.47	0.51	0.5	0.52	0.37	0.91

*OGDYS, dysphagia; OGEAT, eating restrictions; OGREX, reflux; OGODYN, odynophagia; OGPD, pain and discomfort; OGANX, anxiety; Excellent correlation,0.81-1.0; very good, 0.61-0.80; good, 0.41-0.60; fair,0.21-0.40; and poor,0-0.20; All Correlations are significant at 0.01 level (2-tailed)

Table 5. Validity Known Group Comparisons of Differences in Mean Scores (SD) of Scales and Items in the QLQ-C30 and QLQ-OG25 by Stage Tumour and Treatment Intent

QLQ-C30		Stage of tumour				Treatment Intent		
		I&II (n=63) Mean (SD)	III (N=65) Mean(SD)	IV (N=73) Mean(SD)	ANOVA p	Curative (n=166) Mean(SD)	Palliative (n=109) Mean(SD)	T test p
Function scores	PF	64(21)	62(26)	50(25)	0.001	64(23)	49(25)	<0.001
	RF	70(24)	67(27)	55(27)	0.002	68(25)	55(28)	<0.001
	EF	74(17)	73(21)	65(24)	0.027	72(20)	67(22)	0.048
	CF	87(17)	85(22)	79(21)	0.041	84(21)	79(21)	0.136
	SF	57(26)	53(29)	44(28)	0.017	56(27)	45(28)	0.001
	GQL	58(24)	59(26)	47(26)	0.007	57(25)	46(24)	<0.001
Symptom scores	FA	35(20)	36(23)	49(23)	<0.001	37(22)	48(23)	<0.001
	NV	19(25)	20(26)	39(31)	<0.001	20(26)	37(31)	<0.001
	PA	31(20)	37(26)	48(25)	<0.001	34(23)	45(26)	<0.001
QLQ-OG25	OGDYS	18(19)	22(20)	39(26)	<0.001	22(22)	39(27)	<0.001
	OGEAT	30(22)	32(21)	46(26)	<0.001	34(22)	44(26)	0.001
	OGREX	29(25)	29(25)	39(33)	0.003	27(26)	44(26)	<0.001
	OGODYN	23(22)	23(24)	40(30)	<0.001	26(26)	38(29)	0.001
	OGPD	25(22)	25(23)	34(27)	0.004	27(26)	31(26)	0.332
	OGANX	35(30)	39(32)	59(30)	<0.001	36(29)	59(31)	<0.001
	OGEO	19(25)	24(33)	38(34)	0.001	26(30)	35(33)	0.034
	OGDM	38(31)	30(28)	51(31)	<0.001	35(30)	47(33)	0.002
	OGTA	8(18)	11(22)	20(29)	0.016	10(20)	19(27)	0.001
	OGBI	20(27)	22(28)	34(34)	0.012	22(30)	31(30)	0.012
	OGSV	10(19)	11(24)	22(32)	0.009	13(24)	23(29)	0.003
	OGCH	17(25)	18(26)	24(24)	0.218	17(25)	26(25)	0.007
	OGCO	19(24)	22(24)	28(29)	0.097	21(25)	31(28)	0.002
	OGSP	10(21)	11(22)	23(27)	0.002	12(23)	21(26)	0.004
	OGWL	17(25)	19(28)	37(36)	<0.001	19(27)	35(34)	<0.001
	OGHAIR	20(25)	16(23)	25(27)	0.187	17(27)	24(26)	0.12

*QLQ-C30 functional scales (high score=better function): PF, Physical; RF, role; EF, emotional; CF, cognitive; SF, social; GOL, Global Health status/QOL; QLQ-C30 symptoms scales (high score=more problems): FA, fatigue; NV, nausea and vomiting; PA, pain; QLQ-OG25 symptom scales and items(high score=more problems): OGDYS, dysphagia; OGEAT, eating restrictions; OGREX, reflux; OGODYN, odynophagia; OGPD, pain and discomfort; OGANX, anxiety; OGEO, Eating with others; OGDM, Dry mouth; OGTA, sense of taste; OGBI, Body image; OGSV, Saliva; OGCH, Choking; OGCO, Cough; OGSP, speech; OGWL, Weight loss; OGHAIR, Hair loss; a-groups of tumour stage I &II r merged because of small number in stage I(n=6); b-P value derived from ANOVA was used to determine if differences were statistically significant at the 1% level; c-P value derived from t- test which used to determine if differences were statistically significant at the 1% level; d-scores range from 0-100 with higher score indicating better conditions; e-scores range from 0-100 with higher score indicating worse conditions and greater level of symptoms

Discussion

These results present the validation process of Persian version of EORTC QLQ-OG25 which is designed to assess the quality of life of patients with upper GI cancers as a supplement to the EORTC QLQ-C30, which confirm the cross-cultural validity of EORTC QLQ-OG25 in Iranian patients as the second validation report outside the Europe (Onate-Ocana et al., 2012). In other hand, this report is important because of high frequency of upper GI cancer in Iran and recent increasing incidence of oesophagogastric junction cancer in this country (Taghavi et al., 2007; Mousavi et al., 2009; Mohagheghi et al., 2009).

Minor associations between scales in the QOL-C30 and the QOL-OG25 indicate that the specific module (OG-25) addresses different issues from the core questionnaire aspects. The QLQ-OG25 demonstrated acceptable psychometric property and its clinical validity supports its use to supplement the core questionnaire to assess quality of life in patients with different stages of upper GI

cancers undergoing multi-modal treatment either palliative or potentially curative treatments(Lagergren et al., 2007; Onate-Ocana et al., 2012; Tomaszewski et al., 2013).

The multi-trait scaling analysis confirmed six scales (dysphagia, eating restrictions, reflux, odynophagia, pain and discomfort and anxiety) and ten single items (eating with other, dry mouth, sense of taste, body image, saliva, chocking, cough, speech, weight loss and hair loss). Generally, the reliability of the Persian version of the QLQ-OG25 was very good and the reliability (Chronbach's alpha coefficient) of six component of QLQ-OG25 was higher than the originally report (Lagergren et al., 2007) and Onate-Ocana finding (Onate-Ocana et al., 2012), however, similar to those reports, reliability of reflux scale is lower than the other QLQ-OG25 scales in all tumour sites but in gastric cancer in the current study.

The module and core questionnaire were sensitive to clinical differences and were able to discriminate between clinically distinct groups of patients such as patients in different tumour stages and treatment intent groups. Similar finding has been reported in Mexican-Spanish version of the questionnaire (Onate-Ocana et al., 2012) as well as in the original version in English (Lagergren et al., 2007), where the instrument was able to clinically distinguish distinct groups. Although the QLQ-OG25 better distinguished between tumour stages as well as curative and palliative groups, inversely, there was no statistical difference amongst clinically distinct groups except according to tumour site (Onate-Ocana et al., 2012). In the Polish experience with 98 OG cancer patients, no statistical differences were detected in OG-25 scales, (Tomaszewski et al., 2013) which indicate that our findings were superior to the similar studies, which can be attributable to the larger sample size and also more clinically distinction. There was a minor statistical difference in two previous studies in social function, pain and discomfort, eating with other, saliva and speech (Lagergren et al., 2007), pain and discomfort and trouble with coughing (Onate-Ocana et al., 2012), which were dissimilar to our findings. Further studies are also needed to confirm the anticipated sensitivity to change over time in Iranian patients.

After minor changes resulted from patients' opinions in our pilot studies, patient's acceptance was well and we did not notice any problem when it was administered to the Persian language patients who indicated the translation was satisfactory and understandable. As the recent research has shown important advances in neoadjuvant and adjuvant in treatment patients with upper GI cancers (Matuschek et al., 2011; Ku and Ilson, 2012; Xu et al., 2012; Schuhmacher et al., 2013), it was suggested, HRQL measurement evaluated as the most important outcome in oncology patients undergoing different treatment procedure.

In conclusion, the Persian version of QLQ-OG25 has acceptable psychometric properties and is recommended to be administered, together with the core questionnaire, in patients with upper GI cancers. The QLQ-OG25 tool has the capability to distinguish between various treatments modalities, which supports its benefit in routine administration to upper-gastrointestinal (GI) cancer patients.

Acknowledgements

This work was supported by Iran University of Medical sciences (IUMS) as an MSc thesis. The authors greatly appreciate EORTC translation team and the EORTC QLG for their careful, prompt and extensive support of this project. The authors would also like to grateful all patients who participated in this study and officials Omid Oncological Hospital of Mashhad University of Medical Sciences (MUMS).

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