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Oropharyngeal mucositis–specific quality-of-life measure in patients with cancer therapy

Key Messages

1. The oropharyngeal mucositis–specific quality-of-life measure (OMQoL) is the first patient-reported measure specific for oropharyngeal mucositis (OM) and has good reliability and validity. It may be useful for assessing the overall impact of OM from the perspective of patients.
2. The OMQoL may provide a common platform for clinicians to assess, care for, and treat patients with OM.

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Introduction

Oropharyngeal mucositis (OM) is an acute inflammatory and ulcerative oral complication that commonly occurs during cancer therapy. It can cause profound impairment of health-related quality of life (HRQoL).[1] Currently, there is no measure specific to OM that can address health status particularly relevant to OM patients during cancer therapy. The objectives of this study were to develop an OM-specific HRQoL measure (OMQoL) and to evaluate whether its psychometric properties would be adequate to support its use for assessing patients with cancer therapy-induced OM.

Method

This study was conducted from October 2005 to March 2007 in two university-affiliated hospitals and one regional hospital in Hong Kong following approval from their Institutional Review Boards. In accordance with the Declaration of Helsinki, all subjects provided written informed consent before enrolment. Subjects were over 18 years old and diagnosed with haematological malignancies or solid tumours. They were treated with one of the following cancer therapies: stomatotoxic chemotherapy (eg adriamycin, etoposide, melphalan, methotrexate, or 5-fluorouracil), head/neck irradiation, concomitant head/neck irradiation and chemotherapy, or high-dose myeloablative chemotherapy and/or total body irradiation (TBI) followed by haematopoietic stem cell transplant (HSCT). Convenience sampling was used to recruit patients.

The OMQoL was developed and validated in three stages: (1) to perform item generation, (2) to perform item reduction and scale generation, and (3) to assess the construct validity of the developed scale.[2]

Stage 1: item generation

Exploratory, in-depth qualitative interviews were carried out with 23 patients who had experienced OM in order to identify relevant areas, which enabled a large number of candidate questionnaire items to be generated.[3] Three of the investigators independently selected and devised questionnaire items from the qualitative review. All items were formulated both in English and Chinese by a linguistics expert and two bilingual investigators. The degree to which OMQoL elements including individual items, response formats and instructions are relevant to and representative of the targeted construct were determined by focus group discussion (n=13) and expert content review (n=7).

Stage 2: item reduction and scale generation

In order to determine the psychometric properties of the OMQoL, the preliminary version developed in stage 1 was administered to 210 subjects with more than or equal to World Health Organization (WHO) grade-I OM during their cancer therapies to test factor structure, internal consistency and scaling properties. A total of 47 subjects were selected at random to fill in the OMQoL again within 3 days in order to assess the reliability of the OMQoL over time. An exploratory factor analysis was undertaken to extract factors in order to explore how the items of the OMQoL were combined into relevant subscales. Cronbach's alpha coefficient was used to assess the internal consistency reliability for the subscales

total. The test-retest pairs for each individual item were analysed using a Weighted Kappa coefficient,[3] and the test-retest analysis of the subscale total scores was about performed using intraclass correlation.[4] Scale level analysis was evaluated by the floor and ceiling effects, as well as by Rasch analysis.

Stage 3: assessing construct validity

A total of 137 patients completed the OMQoL and the Chinese version of the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30 (EORTC QLQ-C30 [Ch]) in a random order at baseline and twice a week until 3 weeks after completion of stomatotoxic chemotherapy or conditioning regimen for hematopoietic stem cell transplantation (HSCT) [D1, 4, 7, 10, 14, 17, 21, 24, 28], or at baseline and then weekly until 3 weeks after completion of head/neck irradiation (D1, 7, 14, 21, 28, 35, 42, 49, 56, 63, 70), along with concurrent measures of OM using the WHO 0-IV grading system and OM-related symptoms using a 10-cm visual analogue scale.

The mean peak and the area-under-the-curve (AUC) scores for the OMQoL, OM-related pain and symptoms, and EORTC QLQ-C30 (Ch) were calculated prior to construct validity testing, in order to adjust unequal time points of assessments for different cancer therapy groups. Convergent validities were tested by calculating Pearson's correlation coefficient for correlations between the OMQoL subscales and OM-related symptoms peak and AUC scores. Known-groups validity was evaluated by comparing the OMQoL subscale peak and AUC scores among patients with different levels of OM (WHO grade 0, I, II, III, or IV) and different types of cancer therapy, using a one-way ANOVA given normally distributed data.

The responsiveness of the OMQoL to change over time was assessed by comparing the OMQoL subscale change scores among patients with no increment (group A), <2 grades of increment (group B), and ≥2 grades of increment (group C) of OM using the WHO grading system from day 1 to peak, as well as among patients with no reduction (group D), <2 grades of reduction (group E), and ≥2 grades of reduction (group F) of OM from peak symptoms to the last day of data collection. Change of scores in the OMQoL subscales among these subgroups were compared using one-way ANOVA given normally distributed data. The responsiveness of the OMQoL to change over time was also evaluated by relating the OMQoL subscales AUC scores to WHO OM AUC scores using the Spearman correlation test. It was predicted that there would be a moderately high correlation between the OMQoL and WHO AUC scores.

Results

Stage 1: item generation

The mean age of the 11 female and 12 male patients was 42±13 (range, 21-58) years. Nine (39%) patients had nasopharyngeal cancer and seven (30%) had acute lymphoblastic leukaemia. The respondents were well distributed with respect to cancer treatment modality. The analysis of respondent interviews resulted in the generation of 171 items. Three investigators went on to independently select and devise questionnaire items from these 171 items, which were then discussed and scrutinised for repetition and ambiguity until a final set of items was agreed upon. After removal of duplicate and idiosyncratic items, the selection process yielded 63 items for the first version of the OMQoL. Using focus group discussion and expert content review, items were reduced to 41 items. A four-point Likert scale with descriptors (1=not at all, 2=a little bit, 3=quite a bit, 4=very much) response format was selected because previous HRQoL studies indicated this to the most appropriate scoring format for such an instrument.[5]

Stage 2: item reduction and scale generation

The mean age of the 120 female and 90 male patients was 51±12 (range, 21-84) years; 91 (43%) of the patients had nasopharyngeal cancer. Of the 210 patients, 76 (36%) were treated with stomatotoxic chemotherapy, and 71 (34%) with concomitant head/neck irradiation and/or chemotherapy. Patients were quite evenly distributed with respect to OM severity, except for WHO grade IV. Factor analysis of these 41 items resulted in four subscales, which contributed 31 items depicting problems with: symptoms (9 items), diet (10 items), social function (7 items), and swallowing (5 items). As shown in Table 1, the factorial structure was satisfactory with a loading >0.40 on each subscale for all items. Thus, all corrected item scales were higher than 0.40 (r=0.457-0.874). The internal consistency and reliability of each subscale was high with Cronbach alpha coefficients ranging from 0.906 to 0.934. The test-retest reliability of the individual items using Weighted Kappa was good (Kappa values, 0.610-0.895). The intraclass correlation results for the subscale totals were all in excess of 0.70 (0.864-0.934). The floor effect was modest. Rasch analysis supported the present four category scoring system for the OMQoL.

Stage 3: assessing construct validity

The mean age of 65 female and 72 male patients was 49.6±10.9 (range, 18-78) years; 63 (46%) had head/neck cancer. Of the 137 patients, 61 (45%) were treated with stomatotoxic chemotherapy, and 60 (44%) with head/neck irradiation and/or chemotherapy. The frequency of OM was 90%; 11%, 29%, 32%, and 18% had WHO grades I, II, III, and IV, respectively. As shown in Table 2, the OM-related symptom scores correlated highly with the OMQoL, confirming its convergent validity (r=-0.724 to -0.971, P<0.01). Moderate correlations between the subscales of the OMQoL and EORTC QLQ-C30 (Ch) were indicative of good concurrent validity (r=0.450-0.724, P<0.01). The OMQoL could be used to distinguish patients with different OM severities (P<0.01) and types of cancer therapy (P<0.01), providing evidence of good known-group

validity. Patients with OM symptoms who had ≥2 grades of increment from day 1 to peak and ≥2 grades of reduction from peak to the last day of data collection had a larger based on change in OMQoL scores. The changes in effects sizes corresponding to changes in OM curves indicate that the OMQoL is responsive to changes in OM status.

Discussion

Oropharyngeal mucositis can have a significant impact on multiple facets of HRQoL to varying degrees.[1] Clinicians must consider other aspects of OM in addition to about the physical injury. In this era of patient-centred approaches in treatment and care, a better understanding of the HRQoL changes associated with OM viewed from the patient's perspective is needed for informed medical decisions and to improve clinical outcomes. The OMQoL developed in this study addresses experiences judged to be of great importance to patients with OM. Content validity has been addressed by developing items on the basis of in-depth qualitative interviews, focus groups and expert content review.

Our factor analysis supported the creation of symptoms, diet, social function, and swallowing subscales. Such dimensions of OMQoL were distinctive and of special importance in OM. The OMQoL subscales had a high degree of internal consistency, confirming reliability. In addition, the test-test reliabilities were good, meeting all Weight Kappa and intraclass correlation coefficient requirements.[3,4] The symptoms scale consisted of nine items addressing aspects of pain, oedema, burning and bleeding in relation to OM. The diet scale included 10 items assessing different degrees of dietary and eating problems. The social function scale included seven items assessing problems with communicating to others and embarrassment at mealtimes with family and friends. The swallowing scale consisted of five items related to swallowing problems. The present four category scoring system for the OMQoL was found to be valid in terms of Rasch modelling. The floor

Table 1. Exploratory factor analysis and reliability analysis of the 31-item oropharyngeal mucositis–specific quality-of-life measure (n=210)*

Item		
Symptoms		
1	I have swelling inside my mouth	
2	I have mouth ulcer	
3	Mouth pain makes me distressed	
4	I have oozing/bleeding on my lips, or inside my mouth	
5	I feel discomfort while tooth brushing/mouth rinsing	
6	Mouth pain makes me have trouble sleeping	
7	I have mouth pain	
8	I have burning sensation inside my mouth	
9	I have difficulty in opening my mouth	
Diet		
10	I am unable to enjoy food	
11	I reduce outside social dining due to mucosal discomfort	
12	My saliva becomes thick/sticky and need to spit out frequently	
13	I have taste changes	
14	Eating difficulty makes me distressed	
15	I use longer time to drink/eat	
16	I have weight loss	
17	I modify my diet (eg food type, texture and size)	
18	I reduce my soft/solid food intake	
19	I worry about my inadequate nutritional intake	
Social function		
20	I speak with lower quality/voice	
21	I have difficulty in talking	
22	I need to use other means (eg paper/pen, body language) to communicate with others	
23	I feel embarrassed at mealtimes with my family/friends	
24	Speaking difficulty makes me distressed	
25	I do not want to talk to others (including talking on phone) due to mouth discomfort	
26	I have my expression (including smiling to others) and communication affected	
Swallowing		
27	I have throat discomfort	
28	I have difficulty in swallowing liquids (eg water, juice, soup)	
29	I have difficulty in swallowing soft/solid food	
30	I feel easily choked while swallowing	
31	I have difficulty in swallowing saliva	
Explained variance		
Alpha=0.971, standardised item alpha=0.970		

* Loadings >0.30 are presented. Loadings >0.40 are in bold type

effect of the sample was modest, while the ceiling effect was negligible.

The overall correlation coefficients between the OMQoL subscale and OM-related pain and symptom scores were very high (0.724-0.971), confirming the convergent validity of the OMQoL to a high degree. The good convergent validity indicated that the OMQoL can address dimensions of health status that are particularly relevant to patients with OM. Such dimensions of oropharyngeal symptoms and function, nutrition, and social contact were distinctive and of vital importance in OM. Moderate correlations between the OMQoL and EORTC QLQ-C30 (Ch) indicated that these two scales measure concepts that were related but distinguishable and not redundant, thus confirming the concurrent validity.

In addition to convergent and concurrent validities, the construct validity was also supported by comparing the OMQoL subscale scores for sub-populations that varied clinically. Patients with severe OM and those treated with head/neck irradiation and/or chemotherapy scored lower on the OMQoL subscales than patients with mild OM and those receiving stomatotoxic chemotherapy alone. There were statistically significant corresponding changes in scores for the OMQoL subscales among varying levels of changes in WHO OM scores. Additionally, the correlations between changes in the OMQoL subscale and WHO OM AUC scores from day 1 to the last day of data collection were high (0.733-0.877). These results suggest that the OMQoL was responsive to changes over time.

Conclusion

The OMQoL was developed as a patient perspective questionnaire to measure a range of important aspects of HRQOL that can address health status particularly relevant to patients with OM. The OMQoL is reliable and valid and

Exploratory factor analysis				Internal consistency			Test-retest reliability	
Factor 1	Factor 2	Factor 3	Factor 4	Corrected item–total correlation	Cronbach α	α if item deleted	Weighted Kappa	Intraclass correlation
0.550				0.651	0.916	0.910	0.688	0.864
0.645				0.657		0.909	0.718	
0.788			0.346	0.874		0.893	0.754	
0.602				0.457		0.920	0.697	
0.655				0.695		0.907	0.649	
0.525			0.312	0.758		0.903	0.791	
0.868			0.353	0.832		0.897	0.687	
0.569			0.353	0.742		0.904	0.610	
0.448				0.656		0.909	0.792	
	0.802			0.813	0.929	0.917	0.762	0.914
	0.558			0.681		0.924	0.757	
	0.491		0.335	0.680		0.924	0.775	
	0.690			0.621		0.927	0.718	
	0.463			0.822		0.916	0.841	
	0.465			0.745		0.920	0.835	
	0.663			0.598		0.928	0.895	
	0.859			0.802		0.918	0.742	
	0.553			0.729		0.921	0.808	
	0.720			0.745		0.921	0.762	
		0.687		0.785	0.934	0.924	0.726	0.934
		0.640		0.815		0.921	0.826	
		0.742		0.742		0.928	0.698	
		0.528		0.702		0.932	0.722	
		0.726		0.864		0.916	0.895	
		0.715		0.790		0.924	0.786	
		0.680		0.812		0.922	0.800	
			0.642	0.709	0.906	0.896	0.756	0.896
			0.686	0.797		0.878	0.643	
			0.460	0.764		0.886	0.757	
			0.500	0.732		0.891	0.684	
			0.751	0.827		0.871	0.695	
50.258	4.986	4.303	3.252					

Table 2. Convergent and concurrent validities: Pearson correlation between oropharyngeal mucositis–specific quality-of-life measure (OMQoL) and comparator measures (n=137)

Paramter	OMQoL subscale							
	Symptom		Diet		Social function		Swallowing	
	Peak	Area under the curve	Peak	Area under the curve	Peak	Area under the curve	Peak	Area under the curve
World Health Organization OM grade†	-0.090*	-0.733*	-0.863*	-0.844*	-0.856*	-0.843*	-0.872*	-0.877*
OM-related symptoms								
Mouth pain	**-0.945***	**-0.835***	-0.880*	-0.800*	**-0.971***	-0.831*	-0.911*	-0.886*
Throat pain	-0.910*	-0.825*	-0.897*	-0.814*	-0.871*	-0.830*	-0.941*	-0.923*
Difficulty in eating/chewing	-0.921*	-0.825*	**-0.927***	**-0.854***	-0.888*	-0.862*	-0.951*	**-0.943***
Difficulty in swallowing	-0.903*	-0.808*	-0.926*	-0.836*	-0.893*	-0.848*	**-0.959***	**-0.935***
Difficulty in speaking	-0.915*	-0.819*	-0.878*	-0.780*	**-0.941***	**-0.926***	-0.919*	-0.884*
Mouth dryness	-0.844*	-0.724*	-0.872*	-0.763*	-0.821*	-0.766*	-0.885*	-0.852*
EORTC-QLQ C30 (Ch)‡								
Global health status/quality of life	0.547*	0.450*	0.559*	0.531*	0.500*	0.504*	0.514*	0.495*
Physical functioning	0.688*	0.564*	0.719*	0.648*	**0.739***	0.680*	**0.717***	0.641*
Role functioning	0.660*	0.572*	**0.726***	0.601*	0.659*	0.558*	0.686*	0.574*
Emotional functioning	0.665*	0.493*	0.678*	0.641*	0.705*	0.655*	0.645*	0.618*
Cognitive functioning	**0.689***	**0.594***	0.704*	**0.675***	0.724*	**0.731***	0.700*	**0.707***
Social functioning	0.604*	0.495*	0.695*	0.547*	0.633*	0.572*	0.628*	0.554*
Changing of body weight (D1-peak) [n=97]	0.628*	0.683*	0.658*	0.692*	0.636*	0.722*	0.673*	0.734*

* Correlation is significant at the 0.01 level (2-tailed)
† Calculated by Spearman rank correlation; highest correlation coefficients are in bold type
‡ EORTC-QLQ C30 (Ch) denotes Chinese version of the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30

can be used as a HRQOL assessment for cancer patients with OM.

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