Original Article

Assessment of Xerostomia and Its Impact on Quality of Life in Head and Neck Cancer Patients Undergoing Radiotherapy, and Validation of the Taiwanese Version of the Xerostomia Questionnaire

Shu-Chen Lin, MS, RN, Yee-Min Jen, MD, PhD, Yue-Cune Chang, PhD, and Chia-Chin Lin, PhD, RN

Hsin Sheng College of Medical Care and Management (S.-C.L.), Taoyuan; Taipei Medical University (S.-C.L., C.-C.L.), Taipei; Department of Radiation Oncology (Y.-M.J.), Tri-Service General Hospital, Taipei; and Department of Mathematics (Y.-C.C.), Tamkang University, Tamsui, Taiwan

Abstract

The purposes of this study were to (a) explore the impact of xerostomia and saliva flow on quality of life and (b) validate the Taiwanese version of the Xerostomia Questionnaire (XQ) for patients undergoing radiotherapy (RT) for head and neck cancer in Taiwan. This was a prospective longitudinal study. Instruments consisted of the Xerostomia Questionnaire-Taiwan version (XQ-T) and the Medical Outcomes Study Short Form-36 Taiwan Version. Salivary output was measured by collecting unstimulated whole saliva. The questionnaires and measurements of salivary output were completed before RT was initiated and at two, four, six, and eight weeks after RT had started. Changes in xerostomia scores, quality of life, saliva flow, and predictors of quality of life over time were examined by using general estimating equations. The XQ-T is the first xerostomia measurement instrument developed for use with Taiwanese cancer patients and demonstrated excellent reliability and validity. Saliva flow was significantly correlated with XQ-T scores at two, four, six, and eight weeks after RT had started, but not before RT had begun. Saliva flow and quality-of-life scores significantly diminished and xerostomia scores significantly increased over the eight-week period. Saliva flow and XQ-T scores significantly predicted quality of life, after adjusting for the maturation effect. The results of this study show that the XQ-T is the first xerostomia measurement instrument to be developed for Taiwanese cancer patients and demonstrates excellent reliability and validity. J Pain Symptom Manage 2008;36:141–148.

Key Words

Head and neck cancer, quality of life, xerostomia, saliva flow, RT

Address correspondence to: Chia-Chin Lin, PhD, RN, Graduate Institute of Nursing, Taipei Medical University, 250 Wu-Hsing Street, Taipei 110, Taiwan. E-mail: clin@tmu.edu.tw

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Introduction

Head and neck cancer is one of the ten most commonly occurring cancers and accounts for approximately 8% of cancer deaths overall in Taiwan.[1] Radiotherapy (RT) is an effective treatment for head and neck cancer, but because traditional RT treatment fields frequently include the major salivary glands, xerostomia is a common late toxic effect of radiation therapy in patients with head and neck cancers.[2] Almost all patients who undergo RT of the head and neck have some degree of xerostomia resulting from damage to the salivary glands, and this side effect may be acute as well as chronic.[3,4]

Little attention has been given to the problem of radiation-induced xerostomia in head and neck cancer patients in Taiwan, perhaps in part because a valid and reliable instrument for measuring xerostomia has not existed. Effective management of xerostomia is also hampered by the lack of a well-validated, sensitive, and easily-administered measurement tool. Because xerostomia is a subjective experience, assessment of xerostomia must rely on patient self-reports.

The Xerostomia Questionnaire (XQ) was specifically developed to measure xerostomia in head and neck cancer patients. The XQ has been demonstrated to have good psychometric properties.[4] A validated Taiwanese-language version of the XQ will provide a tool to rapidly screen xerostomia in Taiwanese head and neck cancer patients and allow study results to be compared across different countries.

Xerostomia has an effect on several important aspects of a patient's quality of life (QOL).[5] Over the past two decades, there has been a growing and sustained interest in QOL as a secondary end-point in head and neck cancer treatment.[6] However, studies investigating the acute impact of xerostomia on QOL during RT have been lacking. Therefore, the specific aims of this study were to (1) validate the Taiwanese version of the XQ, (2) investigate changes in saliva flow, severity of xerostomia, and QOL during RT, (3) examine relationships among unstimulated saliva flow, xerostomia, and QOL, and (4) explore the impact of xerostomia and saliva flow on QOL for patients undergoing RT for head and neck cancer.

Methods

Participants and Settings

This study used a prospective and longitudinal design and was conducted in the radiology oncology outpatient clinic of a medical center in the Taipei area of Taiwan. A convenience sample was recruited for this study. To be included in the study, patients had to (a) have been diagnosed with head and neck cancer, (b) never have received RT before, (c) be over the age of 18 years, and (d) be able to communicate in Mandarin or Taiwanese. In total, complete data for 50 patients from baseline throughout the course of an eight-week RT treatment were gathered.

Instruments

Instruments consisted of the Xerostomia Questionnaire-Taiwan version (XQ-T), the Medical Outcomes Study Short Form-36 Taiwan Version (SF-36-T), and a demographic and disease information questionnaire.

Xerostomia Questionnaire-Taiwan Version (XQ-T). The XQ was developed by Eisbruch et al.[4] and was found to have good internal consistency, test-retest reliability, and sensitivity for changes in dryness.[4] The XQ consists of eight items, four questions concerning dryness while eating or chewing and four about dryness while not eating or chewing. Patients were asked to rate each symptom on an 11-point ordinal Likert scale from 0 to 10, with higher scores indicating greater dryness or discomfort due to dryness. Each item score was added, and the sum was transformed linearly to produce the final summary score ranging from 0 to 100, with higher scores representing greater levels of xerostomia.

The XQ-T was developed using a translation and back-translation process. The XQ was first translated from English into Taiwanese by a bilingual person. The XQ was then back-translated from Taiwanese into English by a second bilingual person who had not seen the original English version. The two English translations were then compared for consistency. If the back-translated items and the originals were not consistent, the first translator attempted a second translation, which was then compared to the original. This process

was repeated until the back-translated items and the originals were the same.

Saliva Flow. All participants refrained from eating, drinking, smoking, or conducting oral hygiene for a minimum of 90 minutes prior to salivary collection. To avoid diurnal variations in saliva output, all measurements were taken in the morning. Unstimulated whole saliva flow was collected from all participants at baseline (before RT started), and again at two, four, six, and eight weeks after RT started. Unstimulated whole saliva was collected by a spitting method.[7] Participants were comfortably seated and, after a few minutes of relaxation, were trained to avoid swallowing saliva and asked to lean forward and spit all the saliva they produced every 3 minutes through a glass funnel and into a graduated test tube. The volume collected for 18 minutes was measured. The flow rate was determined gravimetrically and expressed in milliliters per minute. The collected saliva was washed at 10 rpm for 2 minutes. Normal flow rate for saliva is between 0.1 and 0.8 mL/min and low flow rate is below 0.1 mL/min.[8–10]

The Medical Outcomes Study Short Form-36 Taiwan Version (SF-36-T). The SF-36 measures health-related QOL, including concepts of physical functioning (10 items), role limitations due to physical health problems (four items), bodily pain (two items), general health (five items), vitality (four items), social functioning (two items), role limitations due to emotional problems (three items), and mental health (five items). The Taiwanese version of SF-36 has been validated in a healthy adult sample.[11,12]

Questionnaire for Demographic and Disease Information. This study included a demographic information sheet containing basic patient information, including age, gender, education, marital status, religious beliefs, and occupation. The disease information sheet consisted of patient diagnosis, medications, treatment status, and whether or not metastasis had occurred.

Procedures

Approval for this study was obtained from the Human Subject Committee of the hospital. Patients who met the selection criteria were approached individually by the research assistant to describe the study and to obtain informed consent. On the day RT was initiated (baseline), the XQ-T, the SF-36-T, the demographic sheet, and the disease information sheet were administered to patients. After patients had completed the questionnaires, unstimulated whole saliva flow was collected. This process was repeated at two, four, six, and eight weeks after RT was initiated.

Statistical Analysis

Descriptive statistics were used to describe the demographic and disease characteristics and the XQ-T, SF-36-T, and saliva flow. Internal consistency was established by calculating the Cronbach alpha coefficient, which ranges from 0 to 1 with higher values indicating less measurement error. The test-retest reliability was evaluated by calculating the paired-*t* tests and the Pearson product moment correlation coefficient between pretest and post-test, with a three-day interval in a sample of 20 patients. Criterion-related validity was examined by calculating the Pearson product moment correlation coefficient between XQ-T scores and saliva flow. Known-group validity was established by comparing the XQ-T score between patients having low saliva flow (< 0.1 cc/min) and high saliva flow (≥ 0.1 cc/min). The study authors hypothesized that patients with low saliva flow would experience more severe xerostomia. Logistic regression was used to perform this test by controlling for the dose effect and the maturation effect.

In addition to the reliability and validity analyses, the Pearson correlation was used to examine the relationship among xerostomia, saliva flow, and QOL. To account for the repeated measurements' dependence, a statistical method called generalized estimating equations (GEE)[13–15] was used to analyze predictors of saliva flow, xerostomia, and QOL. The GEE method also was used to control for the maturation effects (changes in outcome variables resulting from the passage of time).

Results

Participant Characteristics

Characteristics of the 50 patient participants, including disease, treatment, and accumulative RT doses, are presented in Table 1.

Table 1
Demographic and Disease Related Characteristics ($n = 50$)

Characteristics	Mean	(SD)
Age (years)	54.00	14.42
Education (years)	9.58	3.51
RT dose (cGy)		
Two weeks	1587	264
Four weeks	3361	411
Six weeks	5120	479
Eight weeks	6647	500
Prescribed dose	7022	828
	n	(%)
Sex		
Male	42	84
Female	8	16
Marital status		
Married	34	68
Other	16	32
Diagnoses		
Nasopharyngeal cancer	20	40
Oral cancer	20	40
Larynx—hypopharynx cancer	6	12
Salivary gland cancer	4	8
JCC tumor stage		
I	11	22
II	11	22
III	7	14
IV	21	42
T stage		
T1	20	40
T2	12	24
T3	3	6
T4	15	30
N stage		
N0	27	54
N1	10	20
N2	10	20
N3	3	6
Treatment		
RT	16	32
RT postoperative	13	26
RT and CT	19	38
RT and CT postoperative	2	4
RT		
IMRT	32	64
3-D CRT	18	36

SD = standard deviation; RT = radiation therapy; CT = chemotherapy; IMRT = intensity-modulated RT; 3-D CRT = three-dimensional conformal radiation therapy.

Eighty-four percent of the participants were male. The mean (SD) age was 54.0 (14.4) years. The majority of participants were married (68%) and the mean (SD) years of education was 9.58 (3.51). The participants were diagnosed with various types of head and neck cancer. Cancer sites in patients included nasopharyngeal (40%), oral (40%), larynx-hypopharynx (12%), and salivary gland (8%). Forty-two percent of participants were receiving both RT and chemotherapy.

Validation of the Xerostomia Questionnaire-Taiwanese Version (XQ-T)

Internal Consistency. Internal consistency was established by calculating Cronbach alpha coefficients, which were 0.95, 0.92, 0.94, 0.94, and 0.94 before RT and two, four, six, and eight weeks, respectively, after RT had started. The item-to-item correlation coefficients ranged from 0.56 to 0.90 for these eight items.

Test-Retest Reliability. Test-retest reliability was evaluated by calculating the Pearson product moment correlation coefficient and paired *t*-test between pretest and post-test over a three-day interval in a different sample of 20 head and neck cancer outpatients. The test-retest reliability for the XQ-T composite score was 0.96. The test-retest reliabilities of the eight items of the XQ-T over a three-day interval are presented in Table 2.

Content Validity. Content validity was established by a panel of experts. The Content Validity Index developed by Waltz and Bausell was used.[16] The experts were asked to rate each item based on relevance, clarity, simplicity, and ambiguity on the four-point scale. The Content Validity Index was 0.97 for the XQ-T.

Criterion-Related Validity. XQ-T scores were significantly negatively correlated with saliva flow at two, four, six, and eight weeks after RT was initiated. The correlation coefficients were -0.35 ($P = 0.01$), -0.31 ($P = 0.03$), -0.39 ($P = 0.01$), and -0.34 ($P = 0.02$), respectively. The results supported the hypothesis that the XQ-T severity scores correlate with saliva flow.

Known-Group Validity. Consistent with the hypothesis of the study authors, after controlling for treatment sites, accumulated dosage, and time after RT, logistic regression results revealed that patients with low saliva flow (< 0.1 cc/min) reported significantly higher levels of xerostomia severity than patients with high saliva flow (≥ 0.1 cc/min) ($\chi^2 = 39.87$, $P = 0.22$).

Changes of Xerostomia, Saliva Flow, and QOL Over Time

The XQ-T scores, saliva flow, QOL total scores, and the scores of each QOL domain before RT started and periodically after RT

Table 2
Test-Retest Reliability of XQ-T ($n = 20$)

XQ-T Items	Paired *t*-Test	*P*	*r*	*P*
Rate your difficulty in talking due to dryness	0.42	0.68	0.94[a]	0.000
Rate your difficulty in chewing due to dryness	−0.49	0.63	0.96[a]	0.000
Rate your difficulty in swallowing solid food due to dryness	0.00	1.00	0.91[a]	0.000
Rate the frequency of your sleeping problems due to dryness	−0.62	0.54	0.96[a]	0.000
Rate your mouth or throat dryness when eating food	−2.04	0.06	0.98[a]	0.000
Rate your mouth or throat dryness while not eating	−0.49	0.63	0.94[a]	0.000
Rate the frequency of sipping liquids to aid swallowing food	−0.96	0.35	0.94[a]	0.000
Rate the frequency of sipping liquids for oral comfort when not eating	−1.79	0.09	0.96[a]	0.000

[a]$P < 0.05$.

started are detailed in Table 3 and Fig. 1. Changes of XQ-T, saliva flow, and QOL total scores were examined by GEE. After square root transformation due to the requirement of the normality assumption, results revealed that saliva flow and QOL scores significantly decreased and XQ-T significantly increased between preRT and two, four, six, eight weeks after RT started (Table 4).

Interrelationship of Xerostomia, Saliva Flow, and QOL Over Time

The Pearson correlation was used to examine the interrelationship among saliva flow, XQ-T scores, and QOL scores before RT and periodically after RT was initiated. Table 5 shows that saliva flow was significantly correlated with XQ-T scores at two, four, six, and eight weeks after RT started, but not before RT began. XQ-T scores were significantly correlated with QOL scores before RT and at four and six weeks after RT began.

Impact of Xerostomia and Saliva Flow on QOL after Adjusting for the Maturation Effect

Univariate analyses showed that patients with higher RT accumulative dosage and longer time after treatment were found to report significantly lower scores of QOL. The GEE model was used to analyze the impact of xerostomia and saliva flow on QOL after adjusting for the maturation effect. Variables shown by univariate analysis to be related to QOL were entered as independent variables in the GEE model. Results revealed that saliva flow and xerostomia severity significantly predicted QOL for patients with head and neck cancer after adjusting for the maturation effect (Table 6).

Discussion

The use of a subjective measure of salivary function in conjunction with saliva collection has been useful in determining salivary gland dysfunction.[17] However, effective management of xerostomia has been hampered by the lack of a well-validated, sensitive, and easily-administered measurement tool. The XQ-T is the first xerostomia measurement instrument to be developed in Taiwanese for patients with head and neck cancer, and this study is the first one to validate the XQ in a Taiwanese sample of patients with head and neck cancer. The XQ-T shows excellent reliability, validity, and sensitivity, making it a useful tool for assessing xerostomia for clinical as well as research purposes. Reliability was supported by good internal consistency, as demonstrated by the Cronbach alpha and test-retest coefficients. Validity was supported by good known-group validity and criterion-related validity. Patients with low saliva flow reported significantly

Table 3
Mean (SD) Saliva Flow, XQ-T, and QOL Scores Before and After RT ($n = 50$)

	Pre-RT	Two Weeks	Four Weeks	Six Weeks	Eight Weeks
Saliva flow	3.26 (2.36)	1.95 (1.44)	2.04 (1.88)	1.96 (1.74)	2.09 (1.95)
XQ-T scores	9.88 (14.88)	29.86 (18.24)	37.90 (18.74)	44.16 (20.24)	49.04 (20.44)
QOL scores	54.88 (18.02)	49.24 (14.77)	49.47 (15.47)	47.89 (15.51)	45.18 (16.47)

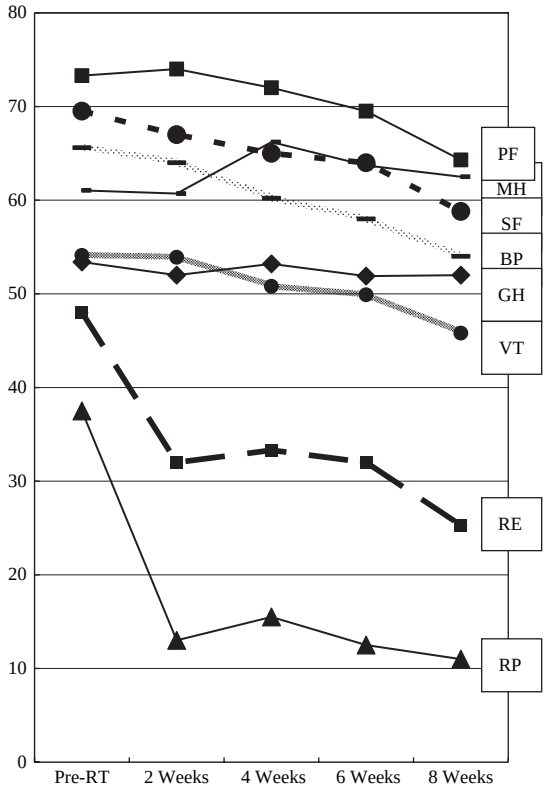

Fig. 1. Changes in quality-of-life domain scores over time. GH = General Health; PF = Physical Functioning; RP = Role Physical; RE = Role Emotional; SF = Social Functioning; BP = Bodily Pain; VT = Vitality; MH = Mental Health.

higher levels of xerostomia severity than did patients with high saliva flow, indicating known-group validity. XQ-T scores were significantly negatively correlated with saliva flow, as measured at different times periodically after RT, indicating criterion-related validity. Sensitivity of the XQ-T was established by the fact that XQ-T scores changed significantly across different time points after RT.

Xerostomia is a significant complaint for patients undergoing RT. This condition is the most common long-term side effect experienced by head and neck cancer patients after receiving RT and contributes to reduced QOL.[18,19] In this study, baseline saliva flow and quality-of-life scores declined and xerostomia scores increased significantly during the eight-week period after RT was initiated. Saliva flow was significantly correlated with XQ-T scores at the different time points at which it was measured after RT had been started. Xerostomia scores were significantly correlated with QOL scores at four and six weeks after RT had been started. These results are similar to the results from the study of Lin et al.,[5] which shows the xerostomia score and QOL score were significantly correlated at 3, 6, and 12 months after RT. However, Fang and colleagues found that there was no statistically significant or clinical changes noted in QOL scores before and one year after RT.[20] In the past, the majority of the literature focused on the late effect after RT and its effect on QOL,[4,5,21] with few studies examining the side effects and impact on QOL during the RT period.

RT for head and neck cancers often affects QOL because of side effects such as salivary dysfunction and xerostomia. This study looked at saliva flow and xerostomia scores and found

Table 4

Changes in Saliva Flow (mL/5 min), XQ-T, and QOL Total Scores (*n* = 50)

Variables/Weeks	Regression Coefficients	Standard Error	Z Value	*P*-Value
Saliva flow				
Two weeks vs. pre-RT	−1.31	0.30	−4.34	< 0.0001[a]
Four weeks vs. pre-RT	−1.22	0.35	−3.51	0.0005[a]
Six weeks vs. pre-RT	−1.30	0.36	−3.61	0.0003[a]
Eight weeks vs. pre-RT	−1.17	0.38	−3.09	0.0020[a]
XQ-T scores				
Two weeks vs. pre-RT	19.98	2.73	7.33	< 0.0001[a]
Four weeks vs. pre-RT	28.02	3.12	8.97	< 0.0001[a]
Six weeks vs. pre-RT	34.28	3.52	9.74	< 0.0001[a]
Eight weeks vs. pre-RT	39.16	3.68	10.64	< 0.0001[a]
QOL scores				
Two weeks vs. pre-RT	−5.65	2.27	−2.49	0.0127[a]
Four weeks vs. pre-RT	−5.42	2.33	−2.32	0.0203[a]
Six weeks vs. pre-RT	−6.99	2.47	−2.83	0.0046[a]
Eight weeks vs. pre-RT	−9.70	3.01	−3.22	0.0013[a]

[a]*P* < 0.05.

Table 5
Interrelationships Among Saliva Flow, XQ-T Scores, and QOL Scores Over Time ($n = 50$)

	Saliva Flow		XQ-T Scores		QOL Scores	
	r	*P*	*r*	*P*	*r*	*P*
Pre-RT						
Saliva flow	—	—	−0.11	0.43	−0.24	0.09
XQ-T scores	−0.11	0.43	—	—	−0.38[a]	0.01
QOL scores	−0.24	0.09	−0.38[a]	0.01	—	—
Two weeks						
Saliva flow	—	—	−0.35[a]	0.01	−0.16	0.27
XQ-T scores	−0.35[a]	0.01	—	—	−0.25	0.08
QOL scores	−0.16	0.27	−0.25	0.08	—	—
Four weeks						
Saliva flow	—	—	−0.31[a]	0.03	−0.14	0.32
XQ-T scores	−0.31[a]	0.03	—	—	−0.42[a]	0.01
QOL scores	−0.14	0.32	−0.42[a]	0.01	—	—
Six weeks						
Saliva flow	—	—	−0.39[a]	0.01	−0.01	0.95
XQ-T scores	−0.39[a]	0.01	—	—	−0.38[a]	0.01
QOL scores	−0.01	0.95	−0.38[a]	0.01	—	—
Eight weeks						
Saliva flow	—	—	−0.34[a]	0.02	0.07	0.61
XQ-T scores	−0.34[a]	0.02	—	—	−0.25	0.08
QOL scores	0.07	0.61	−0.25	0.08	—	—

[a] $P < 0.05$.

them to be predictors for QOL after adjusting for the maturation effect and controlling for other confounding factors in the GEE model. Saliva plays a significant role in taste acuity.[22] However, one study[23] found that QOL declines during RT but recovers to baseline by six months after treatment. In contrast, the xerostomia score increases during RT and does not recover. Ringash et al.[23] concluded that post RT QOL for head and neck cancer patients is independent of xerostomia. Nevertheless, researchers have demonstrated that chemoreceptors on the dorsal tongue anatomy are markedly affected by xerostomia, causing diminished acuity, which, in turn, decreases the ability to taste and, therefore, affects the patient's QOL.[22,24] Moreover, it has been found that subjective and objective salivary gland hypofunction was significantly correlated with vocal dysfunction,[25] which can also contribute to diminished QOL.

Table 6
Predictors of Quality of Life After Adjusting for the Maturation Effect ($n = 50$)

	Regression Coefficients	Standard Error	Z Value	*P*-Value
RT dosage (Gy)	−0.01	0.01	−0.20	0.84
Saliva flow cc/ 18 min	1.84	0.39	4.73	< 0.00001[a]
Xerostomia scores	−0.28	0.05	−5.74	< 0.00001[a]

[a] $P < 0.05$.

The results from this study should be interpreted with caution because of certain limitations. First, we only investigated the impact of xerostomia and saliva flow on QOL for patients undergoing RT for head and neck cancer. The other acute side effects from RT (e.g., pain, mucositis) may be important determinants of QOL in the eight weeks from the start of RT. Second, we did not collect the data on the dose-volume histogram characteristics of the salivary glands. The analysis of salivary gland dose-volume histograms will be useful. Third, we followed patients only during the eight weeks from the start of RT. A longer follow-up period will be needed to understand how saliva flow, xerostomia, and QOL change over time after RT is completed.

In conclusion, the results of our study show that the XQ-T is the first xerostomia measurement instrument to be developed for Taiwanese cancer patients and demonstrates excellent reliability and validity. The XQ-T is a useful tool to assess xerostomia for clinical, as well as research, purposes. Decreased saliva

flow and increased xerostomia scores significantly contribute to impaired QOL after adjusting for other factors. Although this study used a sample of Taiwanese patients with head and neck cancer, it explores a significant human medical condition that is common in head and neck cancer patients in other cultures and provides an important basis for cross-cultural comparisons. Further exploration of interventions aimed at decreasing xerostomia from RT for head and neck cancer patients may ultimately result in significant improvement in patient QOL.

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