

Trismus and reduced quality of life in patients with oral squamous cell carcinoma, who received post-operative radiotherapy alone or combined with chemotherapy¹

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Received 7 June 2017; Accepted 23 August 2017

Abstract: Background: Patients, who receive radiotherapy (RT) for head and neck cancer, develop chronic functional abnormalities and survive with reduced quality of life.

Purpose: We aimed to study patients with oral cancer, who received post-operative radiotherapy or chemoradiotherapy.

Patients: Ten patients (mean age 63.8 years) were included.

Methods: Oral mucositis, pain and xerostomia, maximum mouth opening (MMO) and functional abnormalities before and after RT were recorded. The 35 mm MMO or less was accepted as trismus. Patients completed the EORTC QLQ C-30 and Head/Neck35 questionnaires.

Results: Mean RT dose was 64.3 Gray. Six patients received chemoradiotherapy. Severe mucositis, pain and xerostomia were recorded in 6 and 5 patients respectively. MMO was reduced in all patients. The mean MMO (34 mm) reached the level of trismus. The total number of symptoms increased from 3.1 to 6.3 in C-30 and from 3.1 to 8.8 per patient in the H/N35. Severe fatigue, pain, limitations at work, weakness, sad feelings, family problems, sleeping problems, anorexia, financial difficulties, tense/irritable, constipation, nausea, vomiting and depression were most often reported with C-30. Most patients reported low to moderate quality of life. Severe oral, jaw and neck pain, swallowing problems, taste alterations, sticky saliva, dry mouth, coarseness, dental problems, feeling sick and reduced interest in life/sex were the most common symptoms reported with H/N35.

Conclusions: The observed trismus, 2- to 3-fold increase of symptoms and poorer quality of life highlighted the need for support of oral cancer patients, who receive postoperative radiotherapy or chemoradiotherapy.

Keywords: Oral cancer • Post-operative radiotherapy • Trismus • Quality of life

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¹The study is a part of the Master's Thesis and was approved by the Committee of Ethics for Research of the School of Dentistry, National and Kapodistrian University of Athens, Greece, number 241, 23/04/2014.

Introduction

Oral cancer prevalence is increasing, while the 5 year survival is about 50%. The patients who survive often develop chronic oral complications and functional abnormalities after their oncological therapy [1–4]. Pain in the mouth, jaw and neck, xerostomia/dry mouth, sticky saliva, radiation caries, fibrosis, difficulties in mouth opening and trismus are among the most common chronic complications. Those problems and functional abnormalities are associated with difficulties in food and liquid intake, swallowing problems, with the maintenance of good oral hygiene, speech problems and problems at work, with difficulties in relationships with family and others, and the overall mental, spiritual and physical health. The patient survives with reduced quality of life [5–7]. Quality of life is worse in patients who receive chemoradiotherapy, advanced stage of cancer, with higher dose of radiotherapy and increased radiation toxicity. Quality of life is better when patients can maintain nutrition by normal way [5]. Recent study also reported a similar reduction in the quality of life in the caregivers of the patients, with high levels of stress, mainly related to the feeling of incapacity [8].

Trismus, with reduced mouth opening, is a common chronic complication, which may develop after the completion of RT or months later and increases with increasing radiation doses. A total dose over 60 Grays is related with a higher risk for trismus. The risk for trismus is also increased when the masticator and lateral pterygoid muscles are included in the radiation field, in patients with advanced stage of disease, and with chemoradiotherapy [6,9–11]. Furthermore, patients with oral carcinoma, who receive post-operative radiotherapy have increased risk for trismus, which is related to the fibrosis of masticator muscles due to radiotherapy and due to fibrosis related to the surgical management of tumour [10,12,13].

The purpose of the present study was to assess the development of Trismus and the quality of life in patients with oral squamous cell carcinoma before and after post-operative radiotherapy or chemoradiotherapy.

Patients

Ten patients with oral squamous cell carcinoma were included.

All patients had been pre-treated with surgical removal of their cancer and had been enrolled to receive post-operative radiotherapy alone or combined with chemotherapy.

Methods

All patients signed the informed consent form. They were assessed at 3 time points: before the initiation of RT, at the end of RT, and 3 months after the completion of RT.

Intraoral and perioral clinical examination was performed, with palpation of the masseters and of the other structures of the maxillofacial area. The findings were recorded in the specific forms of the Clinic of Orofacial Pain and the clinical score of Helkimo was assessed [14].

Maximum mouth opening (MMO) was evaluated before and after radiotherapy. The MMO of 35 mm was accepted as Trismus [15].

Patients completed the ten grade visual analogue scale to score pain and xerostomia, while the oral mucositis grade was recorded according to the EORTC/ RTOG criteria [16].

Patients completed the validated questionnaires of EORTC QLQ C-30 and Head and Neck 35 before and after the completion of radiotherapy [17–19].

Results

Epidemiological characteristics

Out of the 10 patients included in the study, nine patients were men and one was a woman, with mean age 63.8 years (range 37-87 years). ECOG performance status was between 0 and 1 [20]. Mean total dose of radiotherapy was 64.3 Gray (available in 8 patients). Six patients received concurrent chemotherapy. The tumour stage (in 7 patients), tumour specific oral site, smoking status and type of chemotherapy (in 3 patients) are also shown in Table 1.

Mean maximum mouth opening

Before the initiation of radiotherapy, 3 patients had trismus, but the mean MMO was high. Maximum mouth opening had reduced from the initiation to the end of radiotherapy in all patients, with mean MMO reduction being 12.1 mm. The mean MMO was 34 mm, thus reaching the level of trismus. Of the two patients who were assessed at 3 months post-RT, one showed complete recovery and the other one with trismus from the beginning of RT showed partial recovery, but remained at the level of trismus. Table 2 shows the MMO for each patient, before, at the end and three months after RT.

Table 1. Epidemiological characteristics of the patients, n = 10.

n	Gender/Age (years)	Disease stage/Site	Smoker Yes/No /Ex smoker	RT/ChemoRT	Total RT dose(Gray)
1.	M/54	T2N0M0/Palate	Ex smoker	RT ²	67,5
2.	M/71	T2N0M0/Buccal mucosa-skin infiltration	Yes	RT ²	61,6
3.	M/77	/Tongue, recurrence	-	RT ¹	-
4.	M/77	T4N0M0/Mandible	No	ChemoRT ²	60,75
5.	M/37	/Floor of mouth, recurrence	No	ChemoRT ¹	-
6.	M/72	/Tongue	No	ChemoRT ¹	60
7.	M/58	T2N0M0/Tongue, recurrence-lymph nodes	Yes	Paclitaxel-Gemcitabine /RT ²	70
8.	M/87	T4N1M0/Buccal mucosa	No	RT ²	61,6
9.	M/65	T3N2M0/Posterior tongue	No	Cisplatin-Platinol weekly /RT ²	67,5
10.	F/40	T1N1M0/Tongue	No	Cisplatin-Platinol weekly /RT ²	66
Mean age 63,8					Mean total dose 64,3 Gy

M = male, F = female, RT = radiotherapy, ChemoRT = chemoradiotherapy, 1 = 3dconformal radiotherapy, 2 = IMRT

Table 2. Maximum mouth opening (MMO), in mm, before and after radiotherapy.

n	Before radiotherapy, n = 10	End of radiotherapy, n = 7	Three months after radiotherapy, n = 2
1.	24	18	
2.	47		
3.	50	43	
4.	36	23	
5.	63	44	62
6.	35	25	31
7.	48	44	
8.	60		
9.	63	41	
10.	35		
Mean MMO 46.1		Mean MMO 34	Mean MMO 46.5

Function of the temporomandibular joint and the score of Helkimo

Increased functional abnormalities were observed. Before radiotherapy 2 of the 10 patients had unilateral sounds and clicking of the joint, while 2 of 8 patients, who were examined after radiotherapy, had similar functional abnormalities. Localized myalgia was observed in 6 of the 10 patients before radiotherapy and in 6 of the 8 patients after radiotherapy. Both patients, who were assessed 3 months after the end of radiotherapy, had muscle sensitivity.

With the Helkimo clinical score before radiotherapy, moderate functional abnormality was recorded in 4 of 10 patients. After the end of radiotherapy, 4 of 7 patients assessed showed moderate and one patient had severe functional abnormality. Three months later, one of the two patients examined had moderate functional abnormality.

Headache

No patient complained of headache before radiotherapy, while 2 out of 7 patients, assessed after radiotherapy, complained of headache.

Table 3. Oral radiation toxicity, end of radiotherapy, n = 10.

n	Oral mucositis (EORTC/RTOG)	Pain (VAS)	Xerostomia (VAS)	Loss of weight (Kg)
1.	II	6	6	
2.	0	0	0	0
3.	III	8	8	
4.	III	7	6	4
5.	III	8	8	9
6.	III	10	10	
7.	III	9	8	
8.	II	5	5	3
9.	III	10	10	10
10.	II	3	0	0

Mean loss 4,3

Table 4. Quality of Life EORTC QLQ-C30, main symptoms with score 3 and 4, before, at the end, and 3 months after radiotherapy.

Symptom	Before radiotherapy, n = 10	End of radiotherapy, n = 8	3 months after radiotherapy, n = 2
Fatigue	5	6	1
Pain	4	5	1
Limitation at work	4	4	
Feeling weak	3	4	1
Feeling sad	3	5	
Family problems	3	4	
Trouble sleeping	2	3	
Anorexia	2	4	
Financial difficulties	2	2	1
Feeling tense	1	3	
Feeling irritable	1	3	
Constipation	1	3	
Nausea/Vomiting		3	
Depression		2	
Total number of symptoms	31 (3,1 / patient)	51 (6,3 / patient)	
<i>Assessment of quality of life (1-7)</i>			
Very poor-poor:1-2	1	2	
Low-moderate:3-4	4	5	1
Good-excellent:5-7	5	1	1

Radiation toxicity

At the end of radiotherapy or chemoradiotherapy clinically relevant oral mucositis, grade III was observed in 6 patients. Severe pain and xerostomia, grade 8-10, were reported by five patients. Mean loss of weight was 4.3 kilograms in 6 patients, who were assessed. Table 3 shows the oral toxicity for each patient separately.

Quality of Life

QLQ C-30

Fatigue, pain and limitations at work, with a score 3 and 4 (much or very much), were the most common symptoms

before RT. However, 5 of 10 patients reported good to excellent quality of life.

At the end of therapy, more patients reported 'much or very much' fatigue and pain, sadness, family problems, sleeping problems, feeling tense and irritable, and having anorexia and constipation. Furthermore, nausea, vomiting and depression were reported for the first time. 5 of 8 patients reported low to moderate quality of life (Table 4).

The total number of symptoms, from the initiation to the completion of RT, increased from 31 to 51 symptoms, showing a 2-fold increase, from 3.1 to 6.3 symptoms per patient.

Three months after therapy, the total number of symptoms was 6 in the two patients who were assessed,

Table 5. Quality of life EORTC QLQ Head and Neck35, main symptoms with score 3-4, before, at the end, and 3 months after radiotherapy.

Symptom	Before radiotherapy, n = 10	End of radiotherapy, n = 8	3 months after radiotherapy, n = 2
Pain in the mouth, jaw, neck	2	8	2
Choked when swallowing		3	
Problems opening the mouth wide	2	2	
Problems swallowing solid food	4	7	1
Problems swallowing pureed food	1	6	
Problems swallowing liquids	3	5	
Problems in conversation	3	6	
Dry mouth	3	5	2
Sticky saliva	4	7	2
Problems with your sense of smell	1		
Problems with sense of taste	4	7	1
Coughing	1	1	1
Problems with social activities	1	2	
Feeling sick		3	
Less physically attractive as a result of disease or treatment	1	4	
Problems talking to other people in public places		1	
Hoarseness	1	2	.
Problems with teeth		2	1
<i>Total number of symptoms</i>	<i>31 (3,1/patient)</i>	<i>71 (8,8/patient)</i>	
Reduced interest for life/sex	5	7	1

with 3 symptoms per patient, as was the case before RT.

Head and Neck 35

Before RT, problems swallowing solid food, sticky saliva and problems with sense of taste were the most often reported symptoms, with a score of 3 and 4. 5 out of 10 patients reported reduced interest in life.

At the end of the therapy, all 8 patients complained of severe mouth, jaw and neck pain as compared to 2 of 10 patients before RT. More patients reported problems swallowing solid and pureed food and liquids, problems with taste, sticky saliva and dry mouth, problems in conversations and social activities and less physical activities. Symptoms like choking while swallowing, feeling sick and dental problems were reported for the first time. Seven of 8 patients reported reduced interest in life (Table 5).

The total number of symptoms showed a close to 3-fold increase from 31 to 71. The ratio per patient increased from 3.1 to 8.8 symptoms per patient.

Three months after therapy, both patients who were assessed, continued to report 'much or very much' pain, with a score of 3 and 4, dry mouth and sticky saliva. One of the 2 patients reported problems with teeth. The total

number of symptoms was 10, with a ratio of 5 symptoms per patient.

Discussion

Trismus

In healthy population, the MMO varies between 41 mm to 52.8 mm [21–23]. Patients suffering from head and neck cancer, an MMO below 35 mm has been defined as trismus, since at this point the patients show functional abnormalities of the maxillofacial structures [15].

The prevalence of trismus in patients with head and neck cancer shows a wide variation in different studies and can be as high as 77%, depending on: (a) the tumour location and tumour stage, (b) the preceding surgical therapy, (c) the oral/maxillofacial structures and the muscles, which have been irradiated, and (d) the total radiation dose [6,9–13]. The absence of specific criteria for the definition of trismus and the non-homogeneous group of patients in the different studies are also some of the main reasons for the above wide variation of the prevalence of trismus in head and neck cancer patients [6,9,12,13].

The 28% prevalence of trismus was reported in a prospective study of 120 head and neck cancer patients. Eighty of those 120 patients had oral or oropharyngeal

cancer. Surgery combined with radiotherapy or chemoradiotherapy were related with reduced MMO. However, the number of patients with oral cancer, who received post-operative RT or chemoRT, was not reported [13]. In a prospective study of a homogeneous group of 143 patients with oral cancer, the prevalence of Trismus at the end of therapy was 44%. The type of therapy was not the same among the patients. Sixty-four of all 143 patients received post-operative radiotherapy [12].

In the present study, a homogeneous group of patients was assessed: all had squamous cell carcinoma and all received post-operative RT or chemoRT. At the end of radiotherapy, a reduction of the MMO was observed in all study patients, as it was reported by others, too [12]. Trismus was observed in 3 of 8 patients (37.5%), while the mean MMO in all patients was below the limit of trismus. The prevalence of trismus was within the range reported in the literature.

Trismus to the head and neck area is related to the total RT dose [9]. Radiation dose equal to or higher than 60 Grays in patients, who had received IMRT, was related with an increased risk for development of trismus. In the present study, the mean radiation dose administered to our patients was 64.3 Grays, which is related to an increased risk for trismus, as reported in the literature.

Functional abnormalities

Sensitivity and myalgia were increased, while functionality of the temporomandibular joints was reduced after the completion of RT. However, the small number of patients did not allow further assessment of significance of those results.

Oral radiation toxicity

Severe oral mucositis was recorded in 6 out of 10 patients in the present study. This toxicity is in agreement with the high (between 40% to 60%) prevalence reported in the literature [24,25].

All 8 patients reported moderate to severe xerostomia after therapy. The symptom was severe in 5 patients. Xerostomia was the most common long-term toxicity reported in the literature. The prevalence can be high as 93% [2,26,27].

Quality of life

EORTC QLQ C-30

The completion and assessment of the questionnaire C-30 showed a worsening of symptoms at the end

of therapy, with a 2-fold increase of the number of symptoms. New symptoms, such as nausea, vomiting, depression were reported for the first time. The findings are in agreement with those in the literature, where the EORTC QLQ C-30 was used [5,28]. Fatigue, anorexia, pain, anxiety and depression were the most common symptoms reported by all the previous authors too [5,28]. In those studies, however, the patients had different head and neck cancers and only some of them had received post-operative RT. In our study, more patients reported low to moderate quality of life after therapy, while fewer patients reported good quality of life.

Three months after therapy, the two patients, who were assessed in our study, showed a trend to systemic health recovery to the initial health scores. The total number of symptoms was 6, with 3 symptoms per patient, as was the case before RT. Although our patients are very few for the assessment of importance of their responses, the findings agree with the literature. Recovery was reported by others as well, starting one month after therapy [5].

EORTC QLQ Head/Neck35

At the end of RT, all patients who were assessed reported an increase in the intensity and the number of oral symptoms. Problems swallowing solid food, soft food and liquids, xerostomia and sticky saliva were common symptoms. Symptoms like choked when swallowing, feeling sick, problems talking to others in public places and problems with teeth were reported for the first time. The total number of symptoms showed a close to 3-fold increase with 8.8 symptoms per patient at the end of RT when compared with 3.1 symptoms per patient before RT. More patients reported reduced interest in life after RT. Dry mouth and sticky saliva were also reported as common symptoms in the EORTC QLQ Head/Neck 35 questionnaire by other investigators [5]. Furthermore, those symptoms were persisting and did not show the same recovery pattern as other symptoms and took more time to improve.

Trismus was an independent and important risk factor for the worsening of quality of life in the several studies and the need for support of oral structures to prevent or manage trismus was highlighted [6,12,13,27,28]. Exercises and specific prevention programs for trismus were prospectively studied but the beneficial result was not permanent for all patients [29–32]. In the present study, using the Head/Neck 35 questionnaire, 2 patients reported problems opening the mouth wide. Most patients, however, reported difficulties in food intake and conversation, which might be related to the restricted mouth opening, which was measured in all patients.

Remission of trismus was seen in 2 of our patients, who were assessed at 3 months after therapy. Lower prevalence of trismus was also reported by others one year after therapy [27]. In contrast, in another study, the remission of trismus one year after the therapy was not observed in the 64 patients who had received post-operative radiotherapy. The authors highlighted the adverse effect of pre-radiation surgery on trismus [12]. In the above study, trismus was not correlated with changes in the quality of life as in the present study.

A moderate compliance of our patients with the study protocol was experienced. At the end of RT, less (8 of 10) patients were assessed, while 2 patients only were examined 3 months after RT. Reduced systemic health, financial difficulties and family problems could be some of the main reasons for this inadequate compliance to the study. Other authors reported inadequate compliance of a large number of patients because of death before the completion of study, refusal for a re-examination, withdrawal from the study, poor systemic health, administrative and technical difficulties [29]. Increased compliance might be achieved with the contribution of the appropriately educated dentist and the support and maintenance of oral health in head and neck cancer patients, as it was shown in the literature [33].

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Conclusions

Reduction of the mouth opening was seen in all patients at the end of therapy, while the mean mouth opening reached the levels of trismus. Quality of life was reduced in all study patients. The need to support the oral structures in patients with oral carcinoma, who receive post-operative RT alone or combined with chemotherapy was highlighted.

The strength of our study was the homogeneous group of patients: all had oral squamous cell carcinoma and all received post-operative radiotherapy or chemoradiotherapy. The small number of patients represents a weakness.

CONFLICT of interest

None

- induced trismus in head and neck cancer patients. *Acta Oncologica* 2016;55:1313-1317.
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